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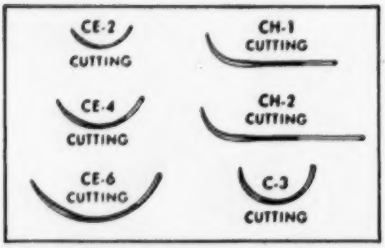

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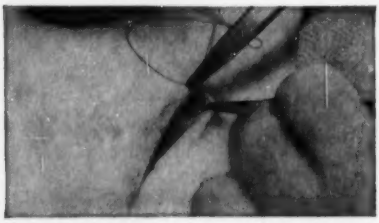

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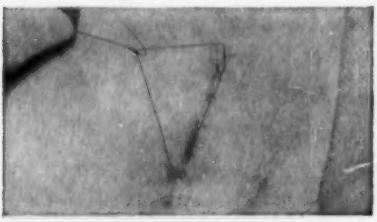

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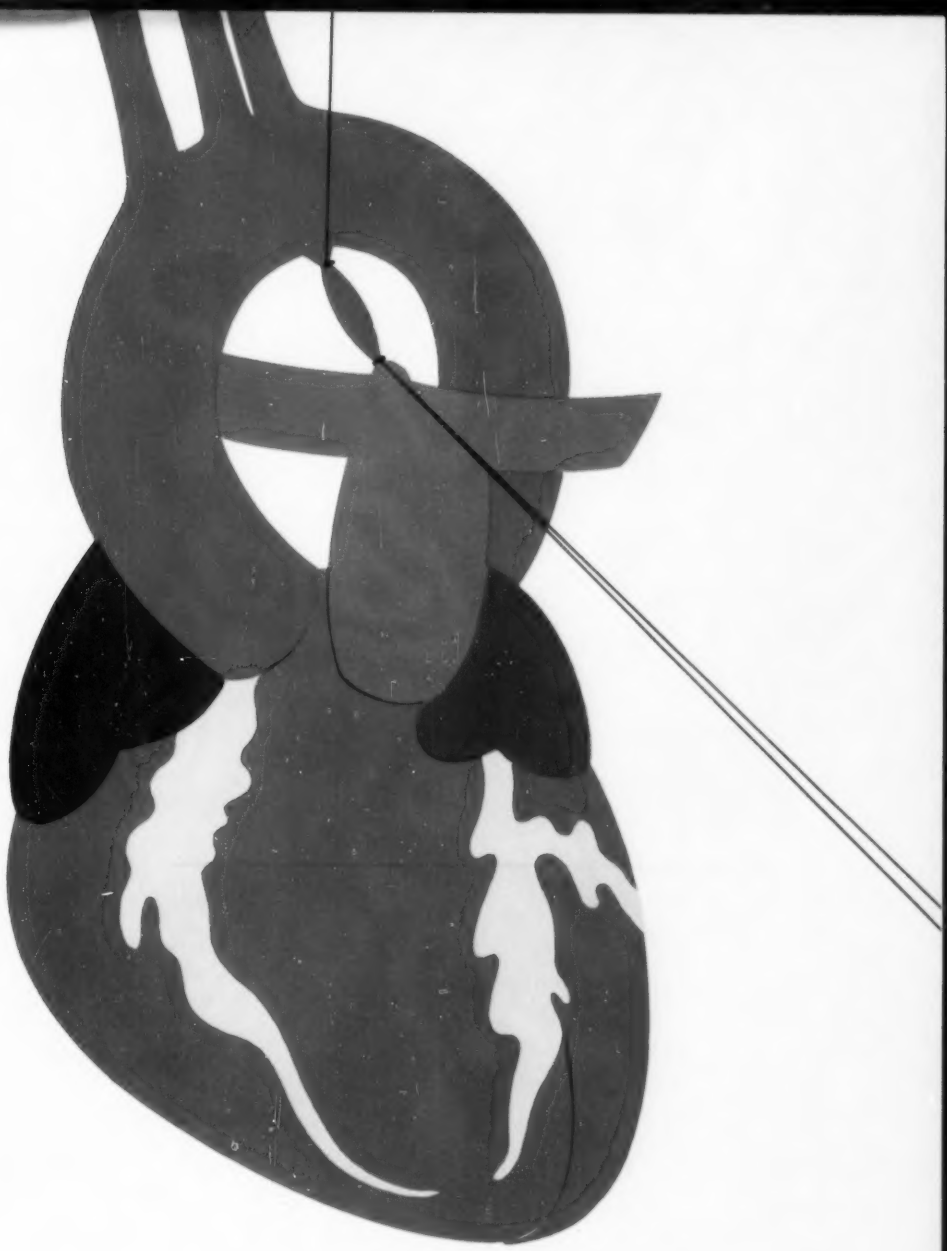

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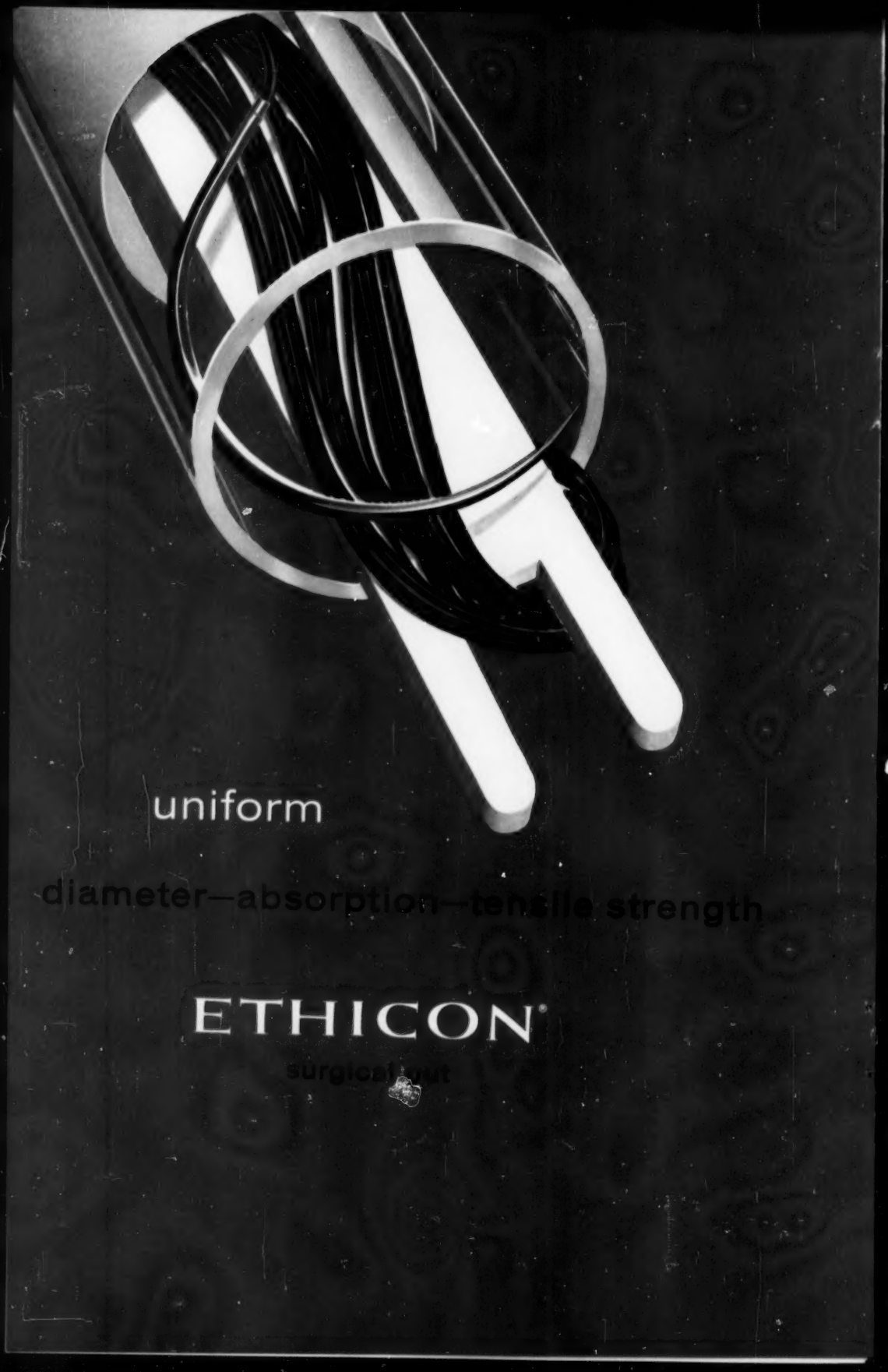
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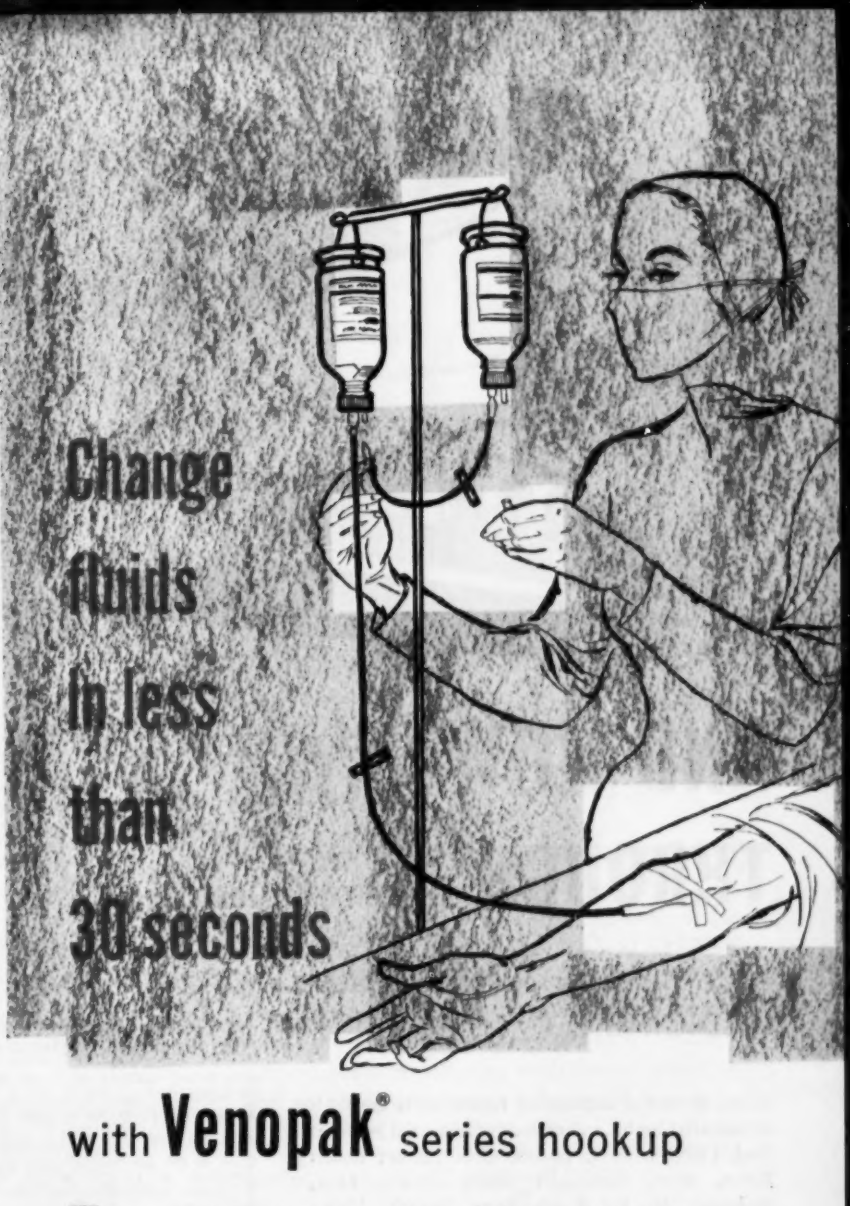

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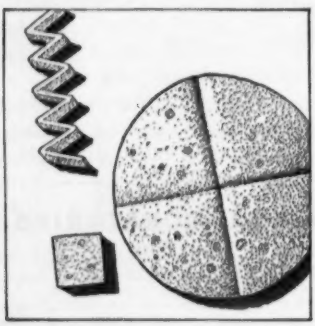

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USE OF CONTROLLED HYPOTENSION IN LARGE BLOOD VESSEL SURGERY

WILLIAM W. L. GLENN, M.D.
L. JENNINGS HAMPTON, M.D.
AND
ALLAN V. N. GOODYER, M.D.
NEW HAVEN, CONN.

CONTROLLED hypotension has been used extensively in this country and abroad as a means of providing a relatively avascular field for surgical procedures. Three general methods of producing hypotension have been used: arteriotomy, total sympathetic blockade by high spinal anesthesia, and ganglionic blockade. Of the three methods the latter is the most physiologically sound and one of the most widely used. Until recently hexamethonium compounds have been generally employed but had the disadvantage of too prolonged vasodilation. Therefore a shorter-acting drug was sought, and recently the experimental and clinical use of a thiophanium derivative * to produce controlled hypotension has been reported.†

Our interest in the use of controlled hypotension as an aid to large blood vessel surgery developed as a result of difficulty in the surgical management of two patients with exceptionally large patent ductus. The experience with one of these patients has been previously reported.[4] In that instance a short patent ductus with a diameter of 22 mm. was found at operation, and it was necessary to reduce the pressure in the ductus by the temporary cross clamping of the aorta proximal to the ductus. About a year later we again encountered a very large ductus in a 20-year-old patient, in whom in addition, the aorta was markedly dilated and thin walled. Division of this ductus was carried out, but just as the suture of the divided ends of the ductus was completed a tear developed in the aorta at its junction with the ductus and at the point of application of the Potts ductus forceps.‡

From the Departments of Surgery and Medicine, Yale University School of Medicine.

This study is a part of an investigation on the use of controlled hypotension in cardiovascular surgery, supported in part by a research grant H-851 from the National Heart Institute of the National Institute of Health, Public Health Service.

* RO 2-2222 (Arfonad); d-3,4[1'3'-dibenzyl-2'-keto-imidazolido]-1,2 trimethylene thiophanium d-camphor sulfonate). This drug was furnished by Hoffmann-LaRoche, Inc., Nutley, N. J.

† References 1, 2, and 3.

‡ The hole in the wall of the aorta was approximately 2 to 3 mm., and hemorrhage was profuse when not controlled by digital pressure. With the aim of closing the tear by the placement of sutures in the aortic wall, the aorta proximal to the ductus was occluded with a Potts coarctation forceps. The points of the clamp penetrated the thin-walled aorta, and hemorrhage occurred at three points in the aortic wall where the forceps was applied. The forceps was quickly removed, and hemorrhage was controlled by digital pressure. At the suggestion of

(Footnotes continued on next page)

Although we considered these two methods of handling large patent ductus therapeutically satisfactory, they were, to say the least, trying and hazardous. It occurred to us after the second case that, should we again be confronted by a large ductus, especially one with a dilated thin-walled aorta, an attempt would be made to reduce the size of the aorta and the pressure in the ductus and aorta prior to division of the patent ductus.

During the past eight months we have used controlled hypotension in seven patients undergoing surgery for a patent ductus (Table). This method was used only in older children or in adults, when the ductus was unusually large and short or the aorta adjacent to the ductus was dilated and thin walled. Hypotension was produced in all but one patient by a constant intravenous infusion of Arfonad in 0.1% solution in 5% dextrose in water. The amount of solution administered was dependent on the response to the drug of the blood pressure of the individual patient, in view of the fact that extreme differences in sensitivity to Arfonad have been observed.[6] The pressure was reduced until there was a visible shrinking of the aorta.

Summary of Data

Case No.	Sex	Age, Yr.	Diagnosis	Operation	Date	Drug	Blood Pressure				Duration,* Min.
							Before	During			
								Low	High	Usual	
1	M	15	P. D. A.	Division	12/ 4/52	Arfonad	152/90	100/68	120/80	120/80	65
2	F	17	P. D. A.	Division	12/11/52	Arfonad	150/80	94/58	120/70	110/60	70
3	M	15	P. D. A.	Division	2/ 5/53	Arfonad	140/64	86/50	106/60	100/60	70
4	M	66	Aortic aneurysm	Resection	5/ 2/53	Arfonad	110/70	70/40	90/50	74/44	80
5	F	33	P. D. A.	Ligation	5/12/53	Arfonad	100/62	70/58	82/50	82/50	15
6	F	14	P. D. A.	Division	6/25/53	Hexamethonium/chloride	144/78	104/70	118/72	110/70	125
7	F	38	P. D. A.	Division	6/30/53	Arfonad	110/60	78/50	90/50	80/50	100
8	F	18	P. D. A.	Division	7/21/53	Arfonad	110/60	84/50	98/58	92/52	65

* Actual period of hypotension. When Arfonad was administered, the blood pressure usually returned to a normotensive level 5 to 15 minutes after infusion of the drug was discontinued. In the one patient receiving hexamethonium chloride the recovery from hypotension was much slower. There was a lapse of one hour after the last dose of hexamethonium chloride (2 mg.) was administered, before beginning recovery of the blood pressure.

It was usually quite easy to maintain the pressure at a constant level (Figs. 1 and 2). In one patient hexamethonium chloride was administered intravenously in increments of 0.5 to 4 mg. for a total dose of 12.5 mg.

In one patient (Case 5) the ductus was ligated rather than divided because of the presence of a large calcified placque that extended from within the ductus lumen almost half way across the posterior wall of the aorta. Suture of the divided ductus in this patient even with the aid of hypotension was considered too hazardous. (This is, we believe, one of the rare indications for ligation of the patent ductus.) The oldest patient in this group (Case 7) was aged 38 at the time of operation. The ductus in this patient was divided in spite of the fact that the aorta appeared to be dilated and sclerotic. Despite hypotension, a tear in the aorta developed at the site of the Potts ductus forceps. Hemorrhage from the aorta was not severe and was easily controlled with absorbable gelatin sponge after approximately 15 minutes of pressure. The aorta was then wrapped with fascia lata as a precautionary measure,

Dr. G. E. Lindskog the aorta was wrapped circumferentially, the fascia lata technique of Wylie and his associates [5] being used. Hemorrhage from all points was immediately controlled, and the subsequent postoperative course was uneventful.

considered advisable to prevent recurrence of hemorrhage from the tear. We believe that controlled hypotension in this patient (Fig. 1), by providing a less distended, more thick-walled aorta, was responsible for preventing a larger tear in this vessel and for making the hemorrhage easier to control. The patient made an uneventful recovery.

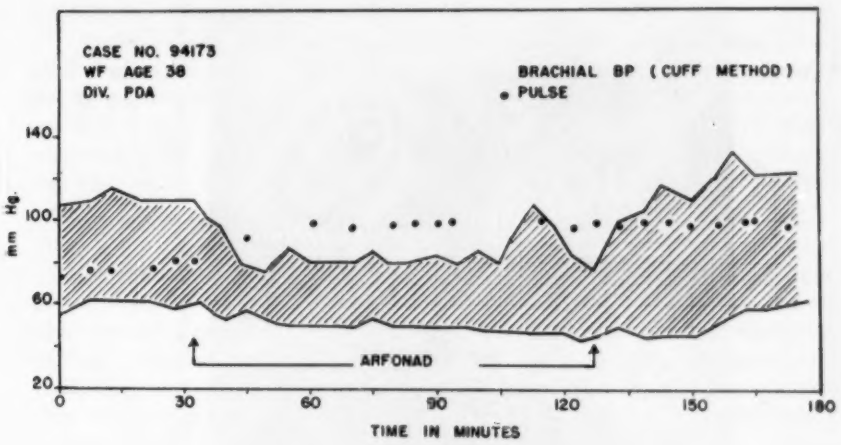

Fig. 1.

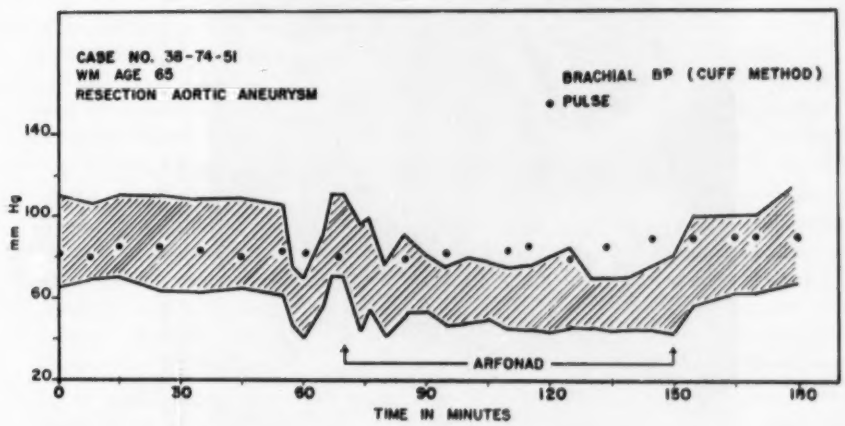

Fig. 2.

Figs. 1 and 2.—Brachial blood pressures taken by cuff method. Values recorded are therefore only approximate. Arfonad, 1% solution, was administered by continuous drip infusion. In Patient 38-74-51 (Case 4) a test dose of Arfonad was given prior to resection of the aneurysm. This is shown on Figure 2 as a sharp fall in blood pressure, with a prompt return to normal.

The excision of aneurysms of the aorta has recently been reported in a number of cases.§ After controlled hypotension was used in several patients with large

§ References 7 and 8.

Fig. 3 (Case 4).—Saccular aneurysm of the ascending aorta: *A* and *B*, preoperative roentgenograms; *C*, postoperative roentgenogram (two and one-half months). Aneurysm has been resected. Nerve palsy is present on left side.

patent ductus, it seemed advisable to employ this technique in the resection of a saccular aneurysm of the ascending aorta (Case 4; Fig. 3). The aneurysm communicated with the aorta through a 7.5 cm. opening. Before hypotension was induced, the aneurysm was tightly distended. After the induction of controlled hypotension (Fig. 2) the neck of the aneurysmal sac became easily compressible. With a Crafoord clamp applied across the neck of the aneurysm, the sac was resected and the opening in the side of the aorta was closed.

Detailed renal function studies were not done on any of these patients, but such routine observations as were made on renal function (PSP, NPN, urinalysis) did not reveal any impairment following operation. Also, there was no evidence of cerebral or coronary complications. The blood pressure was permitted to return to a normotensive level prior to closure of the chest, and there was no evidence at this time or in the postoperative period of delayed hemorrhage from operative wound.

COMMENT

The influence of a hypotensive agent on a dilated and thin-walled aorta is dramatic. It does not require any elaborate experiment to demonstrate the effect of a diminished pressure on the size or wall thickness of a tube with elastic walls. During controlled hypotension the aorta decreases visibly in size and becomes easily compressible between the thumb and forefinger. One fact that seemed remarkable was the decrease in size which occurred after only a moderate reduction (approximately 25%) in blood pressure.

It was of interest to determine whether the pressure in the pulmonary artery might not be affected by the administration of the hypotensive drug, since in patients with pulmonary hypertension the pulmonary pressure could conceivably exceed the aorta pressure, causing a right-to-left shunt as long as the ductus was open. In one patient direct pulmonary artery pressures were taken before and after the ductus was occluded and then again in a similar sequence after the administration of Arfonad. There was a prompt fall in pulmonary artery pressure after the ductus was occluded and an even greater fall with the ductus occluded after the administration of Arfonad. This may have resulted from a decrease in pulmonary vascular resistance due to Arfonad or from decreased venous return and cardiac output,[9] possibly brought about by the creation of a large reservoir for blood in the periphery. The latter mechanism has been suggested to explain the relief by Arfonad of pulmonary edema secondary to pulmonary hypertension in patients with left heart failure.[2] Whether Arfonad has any appreciable effect on the pulmonary artery pressure in the presence of chronic pulmonary hypertension has not been determined.

It would appear from our experience that controlled hypotension as an aid to large blood vessel surgery is a logical procedure, which provides an appreciable decrease in size and easy compressibility of the aorta with only moderate reduction in the aortic pressure. A short-acting vasopressor substance is preferable, particularly when sudden hemorrhage may occur and when suture lines must be tested at normotensive levels.

SUMMARY

Controlled hypotension has been used in seven patients undergoing surgery for closure of a patent ductus and in one patient who had a resection of an aneurysm of the ascending aorta. The impression has been gained that the decrease in size of

the aorta and the ease of compressibility of this vessel resulting from the hypotensive state facilitated the surgical procedures. All patients in this series recovered, and no complications secondary to the hypotensive state during operation were recognized.

ADDENDUM

After this work was begun, a questionnaire was sent out by one of us (L. J. H.) in the course of an investigation on the use of controlled hypotension in the United States. Two instances of the use of controlled hypotension in the surgical treatment of coarctation of the aorta were reported. Unfortunately, the authors of these questionnaires were anonymous; consequently, further details are not known at this time.

More recently, and since this paper was submitted for publication, an article by Julian and his associates [10] has appeared. These authors reported the use of Arfonad to reduce the trauma caused by the aortic hemostatic clamp during the resection of the aortic bifurcation.

REFERENCES

1. Randall, L. O.; Peterson, W. G., and Lehmann, G.: The Ganglionic Blocking Action of Thiophanium Derivatives, J. Pharmacol. & Exper. Therap. **97**:48, 1949.

2. Sarnoff, S. J.; Goodale, W. T., and Sarnoff, L.: Graded Reduction of Arterial Pressure in Man by Means of a Thiophanium Derivative (Ro 2-2222), Circulation **6**:63, 1952.

3. Nicholson, M. J.; Sarnoff, S. J., and Crehan, J. P.: The Intravenous Use of a Thiophanium Derivative (Arfonad-Ro 2-2222) for the Production of a Flexible and Rapidly Reversible Hypotension during Surgery, Anesthesiology **14**:215, 1953.

4. Glenn, W. W. L., and Whittemore, R.: Some Observations on the Surgical Treatment of Congenital Heart Disease, Ann. Surg. **135**:297, 1952.

5. Wylie, E. J.; Kerr, E., and Davies, O.: Experimental and Clinical Experiences with the Use of Fascia Lata Applied as a Graft about Major Arteries after Thrombo-Endarterectomy and Aneurysmography, Surg., Gynec. & Obst. **93**:257, 1951.

6. Little, D. M., Jr., and Hampton, L. J.: Personal communication to the authors.

7. Cooley, D., and De Bakey, M.: Surgical Considerations of Intrathoracic Aneurysms of the Aorta and Great Vessels, Ann. Surg. **135**:660, 1952.

8. Bahnson, H. T.: Definitive Treatment of Saccular Aneurysms of the Aorta, with Excision of Sac and Aortic Suture, Surg., Gynec. & Obst. **96**:383, 1953.

9. Assali, N. S.; Douglas, R. A., and Sugmento, R.: Observations on the Hemodynamic Properties of a Thiophanium Derivative, Ro 2-2222 (Arfonad), in Human Subjects, Circulation **8**:62, 1953.

10. Julian, O. C.; Grove, W. G.; Dye, W. S.; Olwin, J., and Sadove, M. S.: Direct Surgery of Arteriosclerosis, Ann. Surg. **138**:387, 1953.

GASTROINTESTINAL BLEEDING DUE TO SPLENIC VEIN OBSTRUCTION BY PANCREATIC TUMORS

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MASSIVE bleeding into the gastrointestinal tract may be caused by splenic vein obstruction due to involvement of the pancreas by neoplasms, either primary or secondary, or by cysts. Interference with the return flow of venous blood from the spleen may result in congestive splenomegaly, gastric varices, and at times esophageal varices. Fatal hemorrhage from ruptured varices may be prevented in such situations by splenectomy. Recently there have been three patients on the surgical division at this hospital in whom death due to exsanguination was averted by removal of the spleen and the obstructing tumor.

REPORT OF CASES

CASE 1.—M. R. (Montefiore Hospital admission number 53369). The case history of this 51-year-old white man has been reported in detail in a previous publication.[1] Because of massive melena, he had been treated in another institution with repeated blood transfusions. At this hospital he was found to have gastric varices and hypersplenism in addition to severe anemia and tarry stools. On March 3, 1951, through a left thoracoabdominal incision, a splenectomy and hemipancreatectomy were performed for carcinoma of the tail of the pancreas (G. R. G.). Large varicosities were present in the region of the vasa brevia; the spleen was enlarged to three times its normal size, and the splenic vein near the hilus of the spleen was completely surrounded and greatly compressed by the pancreatic tumor. The pathology report was anaplastic adenocarcinoma of the tail of the pancreas and congestive splenomegaly due to extrinsic compression of splenic veins by pancreatic carcinoma.

The postoperative course was uncomplicated, with the exception of a persistent hyperglycemia. For several months postoperatively the patient was able to return to his usual occupation, diabetes was controlled with insulin, and there was no recurrence either of gastrointestinal bleeding or of hypersplenism. Platelet and white blood cell counts remained at normal levels until the terminal episode. Seven months after operation the patient was readmitted to the hospital with intestinal obstruction. At autopsy adenocarcinoma of the body of the pancreas was found with widespread metastases.

CASE 2.—G. C. (Montefiore Hospital admission number 57480), a 46-year-old Italian-born male laborer was admitted to the Montefiore Hospital on March 30, 1952, with a history of intermittent black stools for the previous 15 months. Frequent blood transfusions had been necessary, and massive hematemesis was noted for the first time three months before admission.

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Presented before the Section on Surgery, New York Academy of Medicine, New York, Feb. 6, 1953.

Exploratory laparotomy was performed at another institution on Feb. 20, 1952. At that time the pertinent findings included an enlarged liver, a spleen enlarged to four times normal size, and dilated gastroepiploic veins; the source of bleeding was not identified. A biopsy of the liver was taken, and the pathology report was "pericholangitis."

Melena recurred four weeks after the exploration, and the patient was referred to this hospital with the diagnosis of portal hypertension, for consideration for one of the operations designed to achieve portal decompression. The wound of the previous operation was well healed. There were no palpable organs or masses on abdominal examination. No dilated vessels were seen in the abdominal wall. Esophagoscopy failed to reveal the presence of esophageal varices. A gastrointestinal series of x-rays disclosed an irregularity of the gastric folds in the cardia and fundus of the stomach, compatible with a diagnosis of gastric varices.

On admission the hemoglobin was 7.3 gm. per 100 cc., red blood cell count 2,900,000, and white blood cell count 4,350, with a normal differential smear. Stool guaiac reactions were repeatedly 4+. Liver function tests, including prothrombin time, cephalin flocculation, thymol turbidity, serum bilirubin, and alkaline phosphatase were all within normal limits. The blood urea nitrogen was 15.2 mg. per 100 cc.; fasting blood sugar 111 mg. per 100 cc., and the total protein and albumin : globulin ratio were normal. The patient continued to bleed under observation, with both hematemesis and melena, requiring multiple transfusions. A preoperative diagnosis of a lesion causing localized obstruction to the splenic vein was made on the basis of these findings coupled with the report of an enlarged spleen and dilated epiploic veins found at the previous operation.

On April 29, 1952, an exploration was carried out through a thoracoabdominal incision by one of us (E. S. H.). The liver appeared normal, and the spleen was enlarged to about five times normal size. The gastroepiploic veins and short gastric veins were markedly distended. Venous pressure in a gastroepiploic vein measured 80 mm. of water; in a coronary vein the pressure was 200 mm. of water. It was only after the spleen had been mobilized that a firm round tumor mass was found in the tail of the pancreas, encroaching upon the hilus of the spleen and obstructing the splenic vein. Splenectomy and partial pancreatectomy were performed en bloc. A frozen section of the mass was reported as showing carcinoma of the tail of the pancreas. In an attempt to increase the possibility of radical removal of the tumor, the remainder of the body of the pancreas was removed. During this secondary resection, the superior mesenteric vein was injured, resulting in a massive hemorrhage requiring 23 units of blood transfused under pressure before the hemorrhage was controlled by ligature and packing. Prior to closure of the abdominal wall, the wall of the small bowel was noted to be edematous and slightly blue in color.

The patient's postoperative course was stormy, complicated by paralytic ileus and temporary oliguria. Nasogastric suction was instituted, and the patient received chlortetracycline (aureomycin) by way of the Levin tube as well as streptomycin and penicillin parenterally. He remained in an oxygen tent for two days. Anticoagulants were not given, despite their possible beneficial value in terms of the vascularization of the small bowel, because of the danger of recurrent bleeding from the pancreatic bed. By the third postoperative day the blood urea nitrogen had fallen from 50.5 to 38.8 mg. per 100 cc., and urinary output became normal. Peristaltic sounds were evident, and oral feedings were well tolerated. Glycosuria was present for only 2 days, and did not recur; 10 days after operation the fasting blood sugar was 118 mg. per 100 cc. The stools became guaiac-negative, and the patient was discharged from the hospital two months postoperatively. To date, 19 months postoperatively, there has been no repetition of gastrointestinal bleeding, and there is no evidence of recurrence of his pancreatic carcinoma.

The pathology report was adenocarcinoma of the tail of the pancreas, which was confined to the initial specimen. There was no evidence of malignancy in the body of the pancreas, the removal of which nearly resulted in the loss of the patient. The mass involved the hilus of the spleen, compressing the splenic vein and resulting in chronic passive congestion of the spleen with splenomegaly.

CASE 3.—M. H. (Montefiore Hospital admission number 57222), a 27-year-old white woman was admitted to the hospital on March 5, 1952, with a chief complaint of massive hematemesis. Excision of an enlarged axillary lymph node at another institution two and one-half years prior to this admission had established the diagnosis of Hodgkin's disease. Roentgen therapy had been given, and the patient had done well, until five months before admission, when a persistent hypo-

chromic normocytic anemia was noted. Eighteen days prior to admission the patient had a massive hematemesis, treated supportively with blood transfusions. A second episode of large hematemesis occurred on the day before admission. The patient was hospitalized on the private service of Dr. Okrainetz for management of the gastrointestinal bleeding.

On admission there was no lymphadenopathy, and no abdominal masses could be felt. The hemoglobin was 4.5 gm. per 100 cc.; the red blood cell count, 2,000,000, and hematocrit reading 16%. The bone marrow was hyperplastic. The bleeding, coagulation, clot retraction, and prothrombin times were all normal. The platelet count was normal, and the tourniquet test was negative. A gastrointestinal series and barium enema failed to show any lesion. X-ray examination of the chest revealed a left hilar adenopathy. On the eighth day after admission, the liver and spleen were both palpated 2 fingerbreadths below the costal margin.

The patient was treated supportively with multiple transfusions in the hope that the bleeding would stop. This did happen on several occasions, only to start again. Despite the fact that the source of bleeding had not been demonstrated, an exploratory laparotomy was performed on April 4, 1952. The liver, stomach, and small and large intestine were normal. The spleen was three times its normal size, and the gastroepiploic veins and veins in the vasa brevia were greatly dilated. A large dense mass was found in the hilus of the spleen. The mass was fixed retroperitoneally, at the tail of the pancreas, and could not be resected. It was postulated that the mass represented Hodgkin's disease and that radiotherapy to this area might be beneficial in shrinking the size of the mass, resulting either in cessation of bleeding or in the possibility that the mass might be locally resectable after treatment. Two sets of dilated gastroepiploic veins were ligated and divided in an effort to reduce the venous pressure within the stomach, and the operation was terminated.

Roentgen therapy to the splenic area was instituted on the fourth postoperative day. The patient received a total of 1,200 r over a period of 25 days. During this time she required repeated blood transfusions because of frequent episodes of gastrointestinal bleeding. Esophagoscopy failed to disclose the presence of esophageal varices. One month after operation the mass in the left upper quadrant clinically was smaller.

Forty days after the initial operation (May 14, 1952) reexploration was done through a thoracoabdominal incision (E. S. H.). At this time the spleen was enlarged to about three times normal size, and the mass of tissue around the tail of the pancreas and hilus of the spleen was movable. Splenectomy was performed, together with removal of the tail of the pancreas and the tumor mass. The pathology report was malignant lymphoma with a Hodgkin's type of peripancreatic lymph node involvement and splenic vein obstruction with marked chronic passive congestion of the spleen.

This patient demonstrated no glycosuria at any time. Her postoperative course was complicated by the development of a left subdiaphragmatic abscess, which was drained satisfactorily on the 19th postoperative day. She recovered slowly and was discharged from the hospital two and one-half months after the splenectomy, with no further gastrointestinal bleeding. Since then she has improved remarkably, and at present, 19 months postoperatively, she is able to conduct her daily activities as a housewife and mother. A mass has developed in the right lower quadrant, presumably related to the Hodgkin's disease, and this has been treated satisfactorily by x-ray therapy.

COMMENT

All three of these patients had massive, uncontrollable, recurrent gastric hemorrhages. Definitive diagnoses could not be made prior to surgery. At operation, through a thoracoabdominal approach, all three patients were found to have a tumor mass in the hilus of the spleen, obstructing the splenic vein and resulting in fundal and gastroepiploic varices with gastric bleeding. In all three instances the bleeding was completely controlled by splenectomy and has not recurred to date in the two patients still surviving.

Hypersplenism, as in the first case, has also been reported in a patient with obstruction of the splenic vein by a pancreatic cyst; the abnormal blood picture

was corrected by splenectomy and removal of the obstructing lesion.[2] Rousselot has reported four cases of gastrointestinal hemorrhage due to splenic vein obstruction by benign lesions, including one pancreatic cyst; treatment consisted of splenectomy with excision of the obstructing lesion.[3] The experience in the present series emphasizes his admonition that a thorough search for a locally obstructing lesion be made before a venous decompression shunt type of operation be performed for the relief of the symptoms of portal hypertension. Reliance upon portal venography [4] to define a locally obstructing lesion might have resulted in overlooking the resectable carcinoma of the tail of the pancreas found in our second case. This had been missed at exploratory laparotomy at another institution 64 days prior to operation at this hospital.

Ligation of the superior mesenteric vein during the course of pancreatic surgery, as in the second case in this series, has been accomplished with survival in numerous instances. Orr has summarized these cases recently, giving as a presumptive explanation for survival in some instances the existence of previous partial obstruction of the vein with the development of collateral tributaries.[5] Such was not the case in the present situation. Restoration of the continuity of the vein would be the procedure of choice, and this has been accomplished on a few occasions.* An anastomosis between the mesenteric vein and the inferior vena cava has also been described.[6] At present adequate criteria are not available for the definitive selection of patients in whom it would be safe to ligate the superior mesenteric vein.

It must be emphasized that there is no suggestion in the cases reported of the achievement of a cure. Extraordinary palliation, however, has been accomplished. All three of these patients had required multiple transfusions preoperatively and were in imminent danger of fatal exsanguination. In none of the patients did hemorrhage become a problem postoperatively. The two patients who have survived for 19 months are still completely rehabilitated, one as a manual laborer and the other as a housewife. The woman with Hodgkin's disease is known to have involvement in other parts of her body, and the ultimate prognosis must be that of the underlying lymphoma. The man with carcinoma of the tail of the pancreas has no evidence of recurrence at this time or any untoward sequelae as the result of interruption of his superior mesenteric vein.

SUMMARY

Three cases are presented of massive gastrointestinal bleeding associated with splenic vein obstruction due to pancreatic tumors.

Splenectomy and removal of the tumor obstructing the splenic vein resulted in complete cessation of gastrointestinal bleeding in all three instances.

Carcinoma of the pancreas was found in two cases. One man died seven months postoperatively of recurrent carcinoma. The second man, in whom it was necessary to ligate the superior mesenteric vein, has no evidence of recurrent carcinoma 19 months after operation.

Involvement of the tail of the pancreas by Hodgkin's disease was responsible for the venous obstruction in the third patient.

* References 6 and 7.

In all cases of obstructive splenomegaly with gastric varices and gastrointestinal bleeding, a thorough search for a locally obstructing lesion must be made before performing a venous shunt operation, as for the relief of portal hypertension.

REFERENCES

1. Marks, L. J.; Weingarten, B., and Gerst, G. R.: Carcinoma of the Tail of the Pancreas Associated with Bleeding Gastric Varices and Hypersplenism, Ann. Int. Med. **37**:1077, 1952.

2. Hurwitz, A., and Yesner, R.: Pancreatic Cyst: An Unusual Cause of Hypersplenism, A. M. A. Arch. Surg. **65**:933, 1952.

3. Rousselot, L. M.: Surgical Therapy for Gastrointestinal Hemorrhage in Portal Hypertension, Rev. Gastroenterol. **18**:575, 1951.

4. Rousselot, L. M.; Ruzicka, F. F. Jr., and Doehner, G. A.; Portal Venography: Anatomical and Clinical Studies, Surgery **34**:557, 1953.

5. Orr, T. G.: Some Observations on the Treatment of Carcinoma of the Pancreas, Surgery **32**:933, 1952.

6. Ripstein, C. B., and Ostrow, W.: Gastrointestinal Function Following Radical Pancreaticoduodenectomy, Rev. Gastroenterol. **18**:272, 1951.

7. Moore, G. E.; Sako, Y., and Thomas, L. B.: Radical Pancreaticoduodenectomy with Resection and Reanastomosis of the Superior Mesenteric Vein, Surgery **30**:550, 1951.

8. Child, C. G., III: Surgical Physiology of the Portal Circulation, Presented before the New York Surgical Society, New York, Feb. 13, 1952.

PHYSIOLOGIC AND SURGICAL CONSIDERATIONS IN TREATMENT OF COMPLICATED LESIONS OF BILIARY TRACT

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INTRODUCTION: ARTHUR DEAN BEVAN

THIS AFTERNOON, on my way from the airport, in my memories I ascended the three flights of stairs of the old Rush Medical College building to the large amphitheater in which Arthur Dean Bevan, Head of the Department of Surgery of Rush Medical College, and his medical colleagues, Sippy, Herrick, Post, and others, gave to large classes of medical students a basic knowledge of disease and the art and science of the practice of medicine and surgery.

In the summer of 1917, in the midst of World War I, I transferred from the ivy-covered walls and the whispering pines surrounding the Dartmouth Medical School to the noise and bustle of this great city with all of its opportunities and temptations, accelerated by the uncertainties of war. I had been accepted by two Chicago medical schools as a transfer into their junior classes. I visited clinics at both and was so impressed by the personalities and teachings of Dallas Phemister and Arthur Dean Bevan that I chose to enter Rush, and have never regretted it.

At that time Arthur Dean Bevan was at the height of his career. His influence was great among us students because of his commanding personality and his reputation as a great surgeon and also because of his friendly and understanding contacts with us. He realized the stress and strain that we were under as we tried to complete our medical education while being looked at askance by civilians who wondered why we were not in uniform. I remember that he was one of the members of the Rush faculty who urged that the Army give recognition to medical students preparing themselves for eventual entry into the Army by placing them in uniform, and he was, I believe, partly responsible for the formation of the Student Army Training Corps at the time. On one occasion, at the conclusion of a particularly brilliant operation and a discussion of the indications for the operation, he urged us to invest what money we could in United States War Savings Bonds and then rather shyly said that if any among us couldn't afford to buy a bond, he would be glad to lend us money to do so.

Throughout his long association with Rush, Dr. Bevan maintained his position as head of the surgical staff of Presbyterian Hospital, and he and Sippy and many

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others * not only gave freely of their time in the teaching of their specialties but willingly used their private patients for demonstrations before the students, a contribution which the patients themselves enjoyed making to medical progress. On March 14, 1923, Dr. Bevan performed in Presbyterian Hospital the first operation in which ethylene-oxygen was used as an anesthetic.

In 1929 the Trustees of the Presbyterian Hospital received a million dollar gift from Dr. and Mrs. Bevan for expansion of hospital facilities, particularly for the provision of medical services.

Dr. Bevan was a member of the leading surgical associations of this country, a past President of the Chicago Medical Society, Interstate Postgraduate Medical Association, the American Surgical Association, and also a past President of the American Medical Association.

Dr. Bevan's bibliography, kindly furnished me by Mrs. Helen Molyneaux, Assistant Librarian of Rush Medical College, totals 271 papers. He covered a wide range of subjects in what was truly "general surgery." Among his articles were 25 on the kidney and 20 others on the treatment of such genitourologic lesions as undescended testis, hypertrophy of the prostate, hypospadias, and lesions of the bladder. There were 15 articles on lesions of the biliary tract and 12 on the stomach. I, too, have trod these same surgical fields during my 30 years as a surgeon.

In my years at Rush the internships at Presbyterian Hospital were nonrotating and there were no residencies, as such. However, some outstanding men were kept on as personal assistants to members of the staff and participated in the teaching of the Rush students. From this younger group at Presbyterian and Rush have come great surgeons and leaders in our specialty of surgery. I have no doubt but that the ambitions of many of them were stimulated and aided by Dr. Bevan. Among them were Dean Lewis, Dallas Phemister, Vernon David, Gatewood, Ed Miller, Harry Oberhelman, Herman Kretschmer, and Robert Herbst. It was my good fortune to become intimately acquainted with all of these men years later.

I cannot begin to express my thanks and appreciation to those of you in the Chicago Surgical Society who have invited me to be your guest on this occasion and to give the Arthur Dean Bevan lecture for this year. You have undoubtedly noted the feeling of warmth with which I speak of Dr. Bevan, and I wish to express my gratitude to his associates and those teachers of mine at Rush for the excellent medical and general education which I obtained from them by precept and example. To this was added a delightfully profitable 18 months spent as an intern at St. Luke's Hospital on the rotating services of McArthur, Halsted, and Mock in surgery; Arthur Elliott, Robert Preble, N. C. Gilbert, Joseph Capps and Joseph Miller in medicine, and John Porter and Phillip Lewin in orthopedic surgery. The teaching of these men and that of the physicians at Rush and Presbyterian stood me in great stead during my three-year fellowship in the Mayo Foundation, where additional great men did all in their power to help me enter into a surgical career. It seems rather fitting, therefore, that I should address you this evening on the subject of lesions of the biliary tract, one of Dr. Bevan's major interests, which in these modern days I have tried to give the stimulating title of "Physiologic and Surgical Considerations in the Treatment of Complicated Lesions of the Biliary Tract." This topic has been a major interest of mine since 1921.

* Among these were Herrick, Ticken, Post, Webster, Haney, and Ormsby.

SEARCH FOR KNOWLEDGE ABOUT THE PHYSIOLOGY OF THE BILIARY TRACT

After completing my internship at St. Luke's, I entered the Mayo Foundation as a Fellow in Medicine. I was fortunate to come under the influence of Leonard Rowntree, who, when he learned that I was interested in medical research, suggested that I spend six months in the research laboratory of physiologic chemistry. This experience and the application of the research methods of physiologic chemistry in problem cases stood me in good stead when later I had an opportunity to augment my surgical fellowship by learning experimental methods in surgical research under Frank Mann and Jesse Bollman. During this time, Greene, Snell, and I,[1] following Rowntree's stimulus, began a series of profile studies of liver function in diseased conditions. We hoped to find other tests which would add to the information obtained with the Rowntree-Rosenthal test with the sulfobromophthalein[2] dyes. This led to a particular interest on my part in studying patients with obstructive jaundice.

We were among the first, I believe, to administer dextrose intravenously to improve the function of the liver[3] in such patients. We based our use of it on the experimental evidence of the value of such injections on Mann and on Magath dogs after hepatectomy.[4] At that time bleeding was a serious problem of operations for obstructive jaundice. Following the suggestion of Lee and Vincent, I began to use intravenous injections of a weak solution of calcium chloride which reduced the coagulation time of the blood and did reduce the incidence of fatal postoperative hemorrhage for the many years it was used.[5] This procedure was justly superseded by use of vitamin-K substances, which were introduced clinically by Butt, Snell, and Osterberg.[6] For this they obtained the vitamin-K fraction by extracting it from putrid fish meal with alcohol. Use of vitamin-K substances has almost completely prevented postoperative bleeding in jaundiced patients.

Three other pieces of experimental work about which I feel rather proud were carried out in those periods. These also arose from problems in the management of patients with lesions of the biliary tract. The first concerned a patient on whom I had performed choledochoduodenostomy for stricture of the common bile duct. From a small opening made inadvertently in the stump of the hepatic duct above the point of the anastomosis while dissecting the duct from the liver, large quantities of bile drained into the abdomen the afternoon and evening of the operation. When the incision was opened, bile gushed forth from above the liver; the elevated pulse rate, lowered blood pressure, and increased respiratory rate then returned to normal. The patient recovered. Bollman and I duplicated the condition in the laboratory by inflating a glove placed above the liver of a dog and showed that the changes in pulse rate, blood pressure, and respiration were the result of the displacement and rotation of the liver which interfered with the return circulation through the vena cava to the heart.[7]

A few years later, bleeding from the gall bladder fossa in a jaundiced patient caused blood to accumulate above the liver. When it clotted, the liver was depressed and rotated. Although the patient's condition was extremely serious as a result of the shock-like conditions, the incision was opened and large clots were removed from between the liver and the diaphragm. The patient's condition improved immediately, and she recovered completely. I might say that she had not lost an excessive amount of blood, and loss of blood was not responsible for her shock.

In this regard, Bollman has told me of the studies made during World War II on the cause of blackout among the dive-bombing pilots and among subjects exposed to centrifugal force in the human centrifuge as well as in an airplane dive. In both circumstances some downward drag and partial rotation of the liver occurred, which was partly responsible for the drop in blood pressure and the decrease in the blood draining from the abdomen and lower extremities to the heart, evident in blackout. The blackout or shock-like condition was counteracted in part by the wearing of a very tight abdominal belt which prevented the descent of the liver. More recently descent of the liver has been further prevented by having pilots assume a reclining position.

On other occasions we studied the excretion of bile salts and bile pigment from different lobes of the liver in patients operated on for obstructing lesions of the bile duct.† Of practical importance is the fact that although the estimation of bile salt in the bile is a better indication of hepatic function than the excretion of bile pigment we found that the latter is a rough and reasonably accurate means of determining liver function postoperatively when viewed in light of the total amount of bile excreted.

The problem of biliary dyskinesia in patients having had T-tubes placed in the common bile duct, particularly in cases of spasm of the sphincter of Oddi, was studied by McGowan, Butsch, and myself.[10] We demonstrated by manometric studies as well as by roentgenologic means that spasm of the sphincter of Oddi could be produced by certain agents, such as morphine, which increase the intraductal pressure and produce pain, and could be relieved by such substances as amyl nitrite and glyceryl trinitrate, which relax the sphincter of Oddi.[11] These studies have led us to carry out transduodenal sphincterotomy in some of our patients with biliary colic when no cause for the colic is discovered at operation and the common bile duct is not sufficiently enlarged to permit lateral anastomosis between it and the duodenum.

During this period of study also, I had a chance to observe the death of some patients who were operated on for lesions of the biliary tract in which the picture seemed to be due to hepatic insufficiency. In 1922 Parham and I ‡ reported three cases in which the concentration of the blood urea was decreased as it was in the Mann hepatectomized dogs except that the patient had a progressive decrease in excretion of urine. The clinical picture was similar to that which was described by Gordon Hyde and others, as presented by some patients who died of hepatic failure. I always contended that the hepatic failure in such cases was due to injuries of the blood supply to the right lobe of the liver during cholecystectomy. This, unfortunately, I proved to my satisfaction when I lost a patient as a result of injury of the right hepatic artery in the course of a difficult cholecystectomy. The patient's course, subsequent to operation, was typically that for hepatorenal syndrome in that all the evidences of hepatic failure began to appear on the third day, namely, an increasing jaundice, a decrease in the urinary output, and an increase in the temperature and the pulse rate, with elevation of the blood urea. At postmortem examination partial infarction of the right lobe of the liver was found. There was no injury to the common bile duct.

† References 8 and 9.

‡ In rereading this paper[12] it was most interesting to find the first reference in our bibliography to a paper entitled "Cholemia From Obstruction Due to Common Duct Stone," by A. D. Bevan, appearing in Surgical Clinics of Chicago, **2**:467-473, 1918.

Later on in discussing biliary strictures I intend to comment in more detail on injuries to the hepatic artery as well as to the common bile duct.

SURGICAL CONSIDERATIONS

Clinical study of patients with complicated lesions of the biliary tract provides some of the most interesting problems of study and investigation of human diseases.

The Gallstone in Complicated Lesions.—Most of these disturbances result from gallstones. They develop in the gall bladder, leave it one way or another, and produce complications of biliary obstruction and infection. Although the etiologic factors concerned with the formation of gallstones are not too well understood, the results of their being allowed to remain in the gall bladder and of their leaving it are known to all surgeons but unfortunately are sometimes disregarded by some well-meaning physicians who have concluded that in the absence of symptoms gallstones are not surgical.

With this viewpoint I cannot agree. Indeed, my colleagues and I, at the Mayo Clinic, for the most part advise operation on all patients with gallstones regardless of whether they are producing symptoms, provided that the condition of the patient permits. In my opinion, this viewpoint is amply justified by the fact that for the past few years approximately 25% of our patients at the Mayo Clinic who undergo operations for lesions of the biliary tract have had to have these operations because of complications arising from failure to remove a gall bladder containing gallstones. These complications are well known to all of you—the common duct stone; the the associated pancreatitis and hepatitis; the badly damaged liver, the result of biliary obstruction; acute hydrops of the gall bladder, sometimes with perforation either locally or into the intestinal tract, and postoperative injuries of the bile ducts with their consequences.

To me one of the outstanding things about diseases of the gall bladder is that the symptoms which the patient has are disproportionate to the degree of pathologic changes in the gall bladder. I am sure all of you have seen many patients with seemingly mild attacks of biliary-tract disease, who, at operation, have rather severe inflammation in the gall bladder wall, some of them even have common duct stones.

Recently I operated on a 70-year-old patient who weighed 300 lb. (135 kg.) who came to the clinic after four days of intestinal obstruction due to a gallstone impacted in the terminal ileum. Her only attack of biliary colic occurred 20 years previously! She survived operation, which was made surprisingly easy by having her lie on the left side. The huge panniculus adiposus of the abdominal wall then shifted to the operating table and away from the site of the incision.

The diagnosis of gall-bladder disease made from the patient's history, in my opinion, is much more important than roentgenologic demonstration of the presence or absence of gallstones. This is due to the fact that in at least 15% of our patients who have diseased gall bladders the stones fail to show in the cholecystogram. Although in some of these cases the cholecystogram may show the gall bladder as nonfunctioning, in approximately 10% it does not show the stones and the gall bladder seems to function by filling and emptying. I have seen roentgenologic reports of normally functioning gall bladders in patients from whom I have removed hydropic gall bladders with a sizable stone obstructing the cystic duct. How the dye could get beyond such a stone and make the gall bladder roentgenologically visible is difficult for me to understand, unless the stone obstructed the duct after the cholecystogram was taken.

Stones in Common and Hepatic Ducts.—Before leaving the subject of biliary calculi, I should like to discuss the problem of stones in the common and hepatic ducts. I have governed my decision concerning opening and exploring the common and hepatic ducts on the history of the presence of jaundice and the size of the common duct. If the common duct is enlarged, I open and explore it with flexible scoops of varying size. I began to employ cholangiography [13] about the 12th to the 14th day after operation, in 1936. Since then I have been able to demonstrate that stones will seldom be overlooked if proper exploration of the common and hepatic ducts with scoops and by forcible irrigation is carried out and if this procedure is combined with dilatation of the sphincter of Oddi by passing scoops through it and by palpating the duct, especially the ampullary area, with the scoop *in situ*. I have overlooked a stone in the common duct in only four cases since my return to the Mayo Clinic in 1945, after my Navy service.

That such methods of exploration of the ducts are accurate is evidenced by the fact that neither my surgical colleagues nor I employ cholangiography at the time of operation. I have never seen a common duct of normal size which contained a gallstone. Moreover, because of the reported incidence of error in operative cholangiography,[14] the incidence of pancreatitis [15] reported following its use at the operating table, and because of my satisfaction with the accurate exploration of the common and hepatic ducts, which I have described, I have not used operative cholangiography as an indication for exploration of the common duct. On the other hand, if enlarged common ducts are not opened and explored, even in the absence of a history of jaundice or chills and fever, common duct stones will be overlooked. A study I made several years ago concerning common duct stones removed at operation disclosed that a third of the patients had never been jaundiced, and two-thirds had never had chills or fever.

I have had three cases, two recently, in which blood-stream infections developed after exploration and relief of the obstruction. Two patients had stones in the common duct. One patient had a Proteus infection which responded to a combination of oxytetracycline (Terramycin) given intravenously, dihydrostreptomycin given intramuscularly, and erythromycin given orally. The infection of the other two patients was due to a Gram-negative bacillus of the colon group. This responded to a combination of oxytetracycline and dihydrostreptomycin.

Risk of Operation.—In regard to the risks involved in operations on the biliary tract, I should like to emphasize again the advantage of operating on a patient whose disease is confined to the gall bladder. If a stone is present in the common duct, or if enlargement of the common duct is present, opening and exploring the bile ducts are always necessary.

There is an increase in the operative risk, especially if the patient is jaundiced. This is well illustrated in the Table. The risk of cholecystectomy is increased over threefold for the patient with jaundice over that for the patient without jaundice. This is also true of patients from whom stones are removed from the common bile duct.

Experience with elderly patients has led me to regard operations on them with as little fear as on younger persons, provided the patients in question have been active until the onset of their illness.

I recently dismissed a patient 84 years of age. I had removed several stones from the common and hepatic duct and drained the gall bladder. She was jaundiced prior to operation and the operative risk was considered high. However, she had an uneventful convalescence.

This factor of operative risk has to be considered for patients who have a history of cardiac disease and for those who have had coronary thrombosis three or four months previously. My colleagues, Brumm and Willius,[16] in the study of 257 cases of coronary disease in which operation was performed, reported a mortality rate of 4.3% [11] from cardiac causes. This seems low in the circumstances, yet it must be remembered that this rate is several times that for similar operations on patients without such a history. The crux of the matter, I think, is the ability of the patient to be active without evidences of cardiac insufficiency. Patients who have been up and around and able to carry on their activities, both work and recreation, without too much cardiac embarrassment, are likely to recover from the operation without cardiac complications. Of course, in such cases operation is advised only because of severe symptoms of disease of the biliary tract.

Certain Operations for Benign Lesions of the Biliary Tract, Year 1952: With and Without Jaundice

	Total		With Jaundice		Without Jaundice	
	Operations	Deaths, %*	Operations	Deaths, %*	Operations	Deaths, %*
Cholecystectomy	1,129	0.8	141	2.1	988	0.6
Cholecystostomy	29	13.8	13	7.7	16	18.7
Choledocholithotomy	184	3.3	102	4.9	82	1.2
Choledochostomy	253	0.8	78	...	175	1.1

* Hospital deaths.

Postoperative Complications.—Complications following surgical procedures on the biliary tract usually result from incomplete operations in which common duct stones are overlooked, obstructing lesions in and around the ampulla of Vater or the sphincter of Oddi are not recognized, or association of pancreatitis or hepatitis with an inflammatory lesion in the biliary tract is overlooked. Additional complications follow injuries affecting the blood supply to the liver, usually to the right hepatic artery, and injuries to the common and hepatic bile ducts. Injuries of these structures should not occur. They are usually due to inaccurate exposure of the common and hepatic bile ducts and the hepatic artery and its branches. Injuries to these structures are usually the result of failure of the surgeon and his assistant to understand that cholecystectomy should not be performed until the common and hepatic ducts and the hepatic artery and its branches are identified and the relationship of the common bile and the cystic ducts to each other is determined. This can be done by having the first assistant stretch the portion of the hepaticoduodenal ligament which contains the common duct between the middle and forefingers of his left hand. Then a Deaver retractor is introduced against the liver mesial to the gall bladder, and the structures in the hepaticoduodenal ligament are exposed from the lower end of the common duct to the entrance of the common hepatic duct into the liver.

The number of anomalies of the hepatic artery that exist is unbelievable. I am sure that I have not seen them all as yet. Anomalies of the extrahepatic bile ducts

are rarer. In a few instances I have seen enlarged right and left hepatic bile ducts that joined outside the liver, and recently I saw my first large accessory right hepatic duct which, interestingly enough, contained a gallstone.§ The abnormally located right hepatic duct lay directly in contact with the gall bladder and could have been easily injured if the principle of accurate identification of arteries and duct around the cystic and common ducts preparatory to cholecystectomy had not been followed (Figs. 1 and 2).

Stricture.—This perhaps is as good a place as any to give some over-all observations which I have made in the study of approximately 325 patients with strictures of the common and hepatic bile ducts on whom I have operated since 1924. Follow-

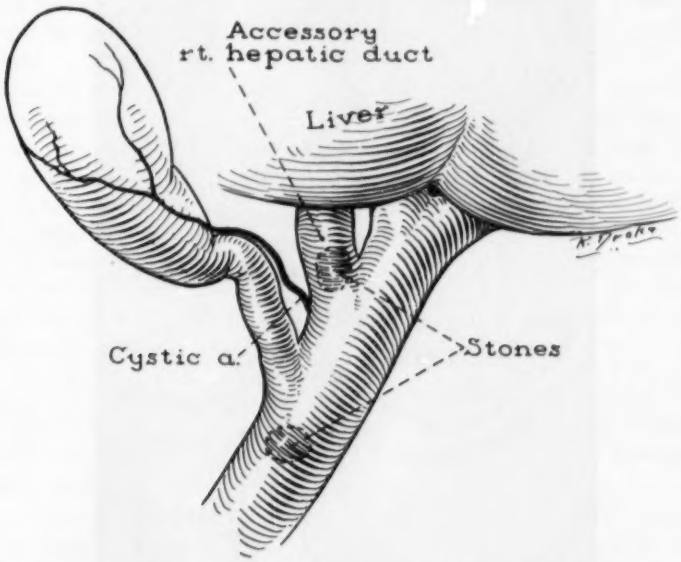

Fig. 1.—Anomalous accessory right hepatic duct with gallstone and stone in the common duct. At operation the gall bladder was in contact with this duct.

up studies in these cases have been made from time to time and the reports published || the last being data presented on 297 such operations performed up to January 1, 1953.[19] From this study I have learned much.

1. In cases of suspected stricture of the common bile duct, it is practically always possible to improve the patient's condition. This is true no matter how many previous operations for repair of the stricture have been performed and whether they were temporarily successful or entirely unsuccessful. Relief of the recurring jaundice may be achieved by anastomosis of extrahepatic bile ducts above the stricture to the intestine or by external hepaticostomy.

2. With increasing experience in the treatment of strictures, it is possible to dissect out a larger percentage of ducts above the stricture than previously. When

|| References 17 and 18.

§ Small accessory ducts lying adjacent to the gall bladder in the gall-bladder fossa are not uncommon.

necessary, the unstrictured portion of the duct can be coned out from the liver parenchyma to anastomose either the duodenum or, in exceptional cases, the jejunum. Likewise, with increasing experience, a greater number of ducts below the stricture can be identified and dissected out for end-to-end anastomosis of the two ends of the duct beyond the stricture.

3. It makes little difference whether one uses a T-tube or an indwelling catheter in cases of ductal anastomosis, provided the tube or catheter is kept in for a sufficient period (usually six to nine months) to prevent contraction at the anastomosis. I have used the T-tube to insure immediate and adequate bile drainage from the liver

Fig. 2.—Postoperative cholangiogram showing the accessory anomalous right hepatic duct.

when the length of hepatic duct remaining for anastomosis to the intestine was very short, when there were stones in the intrahepatic duct together with infection and marked degree of jaundice, and when the patients had marked hepatitis or cirrhosis. The T-tubes provide relief of the biliary obstruction and yet splint the anastomosis. Then, too, after removal of the tube, healing of that portion of the anastomosis through which the external portion of the T-tube has projected does not seem to increase the incidence of recurring stricture of the duct at the anastomosis. This applies particularly to those cases in which the hepatic duct was anastomosed to the duodenum. When sufficient duct has remained for an end-to-end anastomosis, use of the temporarily indwelling catheter with two-thirds of its length

extending into the duodenum, as recommended by McArthur, and the T-tube has been followed by equally good results. The catheter is maintained in place by a long nonabsorbable surgical (silk) suture passed through it and attached to a button on the abdominal wall. Otherwise, intestinal peristalsis will pull the catheter out of the anastomosis.

4. In cases in which biliary intestinal anastomoses have been made to give relief from stricture of the bile ducts, symptoms of recurring pain in the right upper quadrant of the abdomen (with or without jaundice), chills, or fever are the result of varying degrees of obstruction at the anastomosis. Cholangitis is not the result of reflux from the duodenum through the anastomosis into the biliary tract.

5. The postoperative care of the jaundiced patient, with attention to the physiologic needs of the patient, is as important as the methods used in preoperative preparation.

What of the risk of operation for the jaundiced patient who has biliary obstruction due to stricture? Regardless of the degree of jaundice present, I have found that satisfactory results can be obtained with a reasonably low risk, provided hepatic decompensation with ascites is not present. In many cases of varying degrees of cirrhosis, enlargement of the liver, and jaundice, together with rather extensive collateral circulation in the gastrocolic omentum, I have been able to expose the hepaticoduodenal ligament without too much bleeding, regardless of the collateral circulation in the omentum, by dissecting close to the liver. The patients have survived their operations, usually have been relieved of the jaundice, and have improved function of the liver. In some of these cases, it has taken me an hour or more to stop the bleeding from the innumerable branches of these collateral veins before being able to attack the problem of the extrahepatic biliary obstruction. When patients with stricture also have hepatic decompensation, even though the extrahepatic biliary obstruction is relieved at operation, the patient is likely to die of hepatic insufficiency in the weeks that follow operation.

When accurate duct-to-duct or duct-to-duodenum anastomosis has been carried out, 75 to 80% of patients have attained excellent results. The risk of operation has averaged 5%.

Time does not permit a detailed discussion of the postoperative complications that may occur in the jaundiced patients nor of the successful procedures that have been employed for relief. However, I should like to present one case as an example of one of the complications which may occur.

The patient had had cholecystostomy in 1946 and cholecystectomy in February, 1952. He was well 11 months after the latter. Then he noticed itching, dark urine, pale stools, and that his eyes were yellow. Thereafter, he had intermittent jaundice and lost 6 lb. (3 kg.) in three months.

The patient came to the clinic in April, 1953. His condition was diagnosed as incomplete stricture of the common duct, and a choledochoduodenostomy was performed over Mayo-Sullivan tube on April 25. On May 9, it was necessary to incise and drain bile from the pelvis. He was dismissed from the hospital on May 28. In the next week, temperature varied between 99 and 101 F., and then purulent drainage began from the lower angle of the wound. A right subdiaphragmatic abscess was incised and drained. The incision healed, and the patient returned home in three weeks.

Another complication which may occur is bleeding. The introduction and use of vitamin K in jaundiced patients have reduced the incidence of postoperative

bleeding to an almost minimal degree, except in cases in which branches of the hepatic artery have been injured in the course of operations on the bile ducts. On a few occasions, I have found ligatures in the wall of the right hepatic artery in the course of operations for strictures of the common bile duct. It seems obvious in these cases that injury of the duct had probably occurred at the time of the repair of the injury to the right hepatic artery.

One of my most interesting cases of this type was that of a man on whom I resutured a right hepatic artery injured at the previous operation when the common duct was injured and performed double hepaticoduodenostomy for the repair of his stricture.[19] Severe intra-abdominal hemorrhage ocurred from the artery eight days after operation, necessitating disruption of the double hepaticoduodenostomy with control of the bleeding from the artery by suture and forceps application. The opening in the duodenum was closed and the ends of the duct were left open. The curved hemostats on the right hepatic artery were removed 72 hours later, without further bleeding, and spontaneous biliary intestinal anastomosis established itself in 30 days.

I have seen the spontaneous development of biliointestinal communications in other cases. Marvin and I [20] have reported several. However, it was necessary to reoperate in many of these cases later to relieve recurring biliary obstruction, but at this later time the jaundice had lessened and the condition of the patient had so greatly improved that sufficient time could be taken to find the stump of duct beyond the stricture and anastomose it accurately to the intestine.

Biliary Dyskinesia.—What are the problems that exist in the treatment of pain from lesions of the biliary tract or in the relief of attacks of pain in the right upper quadrant that simulate the pain of such lesions? I am referring to that group of conditions called by some physicians the "postcholecystectomy syndrome" and by others "biliary dyskinesia." I have seen many of these patients and, without exception, have advised exploration of the common bile duct when attacks of pain are severe and have been increasing in frequency and severity. I do this because most of these patients have lesions which are demonstrable at operation. The lesions consist most frequently of overlooked or recurring stones in the common or hepatic bile ducts, an elongated cystic duct, or pancreatitis. In some cases a remnant of infected gall bladder remains. In a few cases perforating duodenal ulcers on the posterior wall cause symptoms which simulate those of biliary colic, even to the extent of producing mild degrees of jaundice. These symptoms are due to inflammation in the head of the pancreas which in turn compresses the pancreatic portion of the common bile duct. It is difficult for the roentgenologist to demonstrate such duodenal lesions unless the crater of the ulcer is seen. In most cases of pancreatitis which I have seen and been able to identify at operation, there has been either a thickening and enlargement of the head of the pancreas or the pancreas has contracted in length, has become small and circular, and has resembled a piece of rope more than normal, flattened, soft, irregular tissue. Then there are cases of idiopathic biliary dyskinesia in which the common bile duct may or may not be enlarged and in which in the absence of a stone in the common duct or pancreatitis the assumption is that the patient's attacks of pain are the result of spasm of the sphincter of Oddi.

Unfortunately, prior to operation, there is no way to determine the cause of the attacks of pain, for common duct stones rarely show themselves on roentgenologic examination of the right upper quadrant of the abdomen. I have been told by one of my colleagues in the section of roentgenology that there is now a new dye which

is excreted in the bile in such concentration that a fair image of the common bile duct is obtained roentgenographically. I have had no personal experience with the use of this dye in any case.

Without doubt, spasm of the sphincter of Oddi occurs in certain cases of biliary dyskinesia and its relief by transduodenal sphincterotomy seems a worthy surgical procedure. I have used this procedure in a few cases but without entirely complete success from the standpoint of relief of the patient's pain. In one case in which I used a short T-tube, postoperative roentgenologic visualization of the extrahepatic bile ducts gave evidence of narrowing of the duct above the sphincter, probably from the pancreas. When the common bile duct has been enlarged in such a case and when common duct stones were not present, I have done lateral choledochoduodenostomy with varying degrees of success. In some of the cases I have left a Mayo-Sullivan rubber tube in the anastomosis. I have maintained it in position with a silk suture passed through it and carried to the outside of the abdomen where it was fastened to a button. This enabled me to determine that pain following operation, should any occur, was not due to an increase in intraductal pressure because of possible occlusion of the anastomosis, for with the Mayo-Sullivan tube in place, bile passed through and around it into the duodenum.

Kenneth Starr, of Sydney, Australia, in a Mayo Foundation lecture, advocated sphincterotomy with catheterization and dilatation of the pancreatic duct at its entrance into the ampulla as a means of relieving attacks of pain after cholecystectomy. In a series of cases he found stenosis of the pancreatic duct at its entrance into the ampulla of Vater. When the opening was dilated forcibly, dilatation of the pancreatic duct with retention of pancreatic fluid behind it could be demonstrated. Such procedures were followed in most cases by relief of the attacks of pain. In my own experience, it has been difficult to identify the opening of the duct of Wirsung even when the interior of the ampulla was exposed well.

I have no particular suggestions to make as to a further solution of this problem. I doubt if resection of the head of the pancreas with reimplantation of the head of the pancreas into the intestine is the answer, for then an operation of considerable magnitude is used in cases with uncertain diagnosis and, I fear, with uncertain results. Moreover, I think that whether sphincterotomy, choledochoduodenostomy, or both, are the solution to the problem will not be determined until a sufficient number of these operations have been performed and results have been studied for a long period. In some cases in which both choledochoduodenostomy and sphincterotomy have failed to relieve attacks of pain, injection of the splanchnic nerves with procaine hydrochloride and in some cases cutting the splanchnic nerves have been followed by surprisingly good results. Unfortunately this does not occur in every case. The explanation for these varying results probably is that the causes of the attacks of pain are variable, and some undoubtedly are the abdominal manifestations of psychoneurosis. In the absence of common duct stones, spasm of the duodenum or the sphincter of Oddi, or pancreatitis may cause the pain. To determine which one is responsible will require accurate diagnostic methods in each case. Methods for use in suspected cases of pancreatitis are not yet accurate enough to be diagnostic.

At present, then, our program is to advise exploration of the common bile duct in such cases in the hope that a cystic, common, or hepatic duct stone will be found. If there is uncertainty concerning the presence of pancreatitis and if the common

bile duct is enlarged, a lateral anastomosis is made between the common duct and the duodenum. In some cases a piece of rubber catheter of the Mayo-Sullivan type is kept in the anastomosis for a time. Use of this procedure depends on the size of the duct. If the common duct is large, the splint is not used. When it is small, transduodenal sphincterotomy is done and an attempt is made to identify the pancreatic duct and catheterize it if possible. In my early cases I used long T-tubes of the Cattell type after sphincterotomy. The long arm of these was extended through the sphincter and ampulla into the duodenum. In two cases in which such T-tubes were allowed to remain for more than three months the patients continued to have attacks of pain. These probably were the result of partial obstruction of the exit of the pancreatic duct into the ampulla. At any rate, pain was relieved after removal of the T-tube. Recently, I have used shorter T-tubes which extend only about an inch into the duct. These have permitted study of the function of the common duct, particularly its lower end. If attacks of pain occur while the T-tube is in place and spasmodic contraction of the sphincter is prevented by sphincterotomy, the pain obviously is not due to an increase in intraductal pressure. On the other hand, the long tube extending through the incised sphincter of Oddi may prevent it from scarring down, which otherwise might occur, and may possibly produce the biliary stasis that the operation is aimed to prevent.

Malignant Disease of the Bile Ducts.—No discussion of complicated lesions of the biliary tract is complete without some comment on malignant disease of the bile ducts. Fortunately such lesions are not common. When they occur, they are situated more frequently in and around the ampulla and papilla of Vater than at either of the bifurcations of the extrahepatic duct system. When a lesion involves the lower part of the duct, and is large, it is readily palpable at operation.

On two occasions I have identified an ampullary lesion by scraping the region with a scoop to obtain small pieces of tissue which on microscopic examination showed papillary carcinoma. In most cases, however, such specimens cannot be obtained and it is necessary to open the duodenum to ascertain the presence or absence of papillary carcinoma. Landry and I reported several such cases.[21] It is frequently advisable if jaundice has been or is present, therefore, to open the duodenum in cases in which the common duct has been obstructed and at operation is found to be enlarged and no explanation is found for the obstruction. By this procedure it is possible to ascertain that an early ampullary or periampullary lesion is not present. If no lesion is found at the ampulla, sphincterotomy can be done if advisable. If findings indicate pancreatitis or narrowing of the duct above the sphincter, lateral choledochoduodenostomy can be performed. The treatment for ampullary lesions is, of course, radical resection of the Whipple type.

The possibility of a papillary lesion of one of the intrahepatic ducts was recently called to my mind by a patient on whom I operated.

The patient, a woman, 79 years of age, had had pernicious anemia and combined degeneration for many years. About eight months before registration at the clinic several attacks of chills and occasional vomiting occurred without jaundice. Then she had a shaking chill and fever of 103 F., with vomiting, prostration, and generalized abdominal pain. Examination disclosed hepatomegaly and splenomegaly.

Laboratory examination at the clinic revealed 64 units of amylase, 1.4 mg. of direct-reacting and 0.5 mg. of indirect-reacting bilirubin per 100 cc. of serum. Blood cultures were negative. The cholecystogram disclosed a nonfunctioning gall bladder, and results of a second roentgenologic examination of the gall bladder were indeterminate. Cholecystectomy and choledochostomy

were performed for papillary adenocarcinoma confined to the left hepatic duct. The intraductal portion of the lesion was scraped away. The postoperative course was uneventful, and the postoperative cholangiogram showed normal conditions. The patient was dismissed in three weeks.

The postoperative cholangiogram (Fig. 3) showed no evidence of the neoplasm. The infiltrating type of lesion in this vicinity, however, can be recognized only by the unexplained narrowing of the duct. Some time ago I operated on such a patient. Recognizing the possibility that the narrowing in the left hepatic duct could be due to an infiltrating carcinoma of the wall of the duct, I placed the upper part of the T-tube through it and allowed it to remain for several months. The patient then became jaundiced. The T-tube was removed in the hope that the clinical diagnosis

Fig. 3.—Postoperative cholangiogram showing seemingly normal left hepatic duct after removal of intraductal portion of a papillary carcinoma.

of neoplasm might be in error, that the lesion was an inflammatory one and the T-tube might be partially occluding the duct. Unfortunately, jaundice deepened. An inoperable carcinoma of the common and hepatic ducts was found at exploration. This type of lesion is, in my opinion, inoperable.

The difficulty of determining whether such intrahepatic ductal narrowing is inflammatory or malignant is further evidenced by the next case.

A woman, aged 47 years, first had distress when she was 11 years of age. When 16 years old she had attacks of fullness and bloating and severe steady pain in the midepigastrium extending to the back. In 1931 cholecystectomy was performed elsewhere for gallstones. T-tube drainage was carried out for one month, and bile drained copiously for one month after removal of the T-tube. From time to time the patient had fullness in the epigastrium. From 1946 to 1952

attacks occurred every two months, then every three weeks. Aching of the entire body, fullness of the abdomen, chills, fever to 102 F., vomiting, and jaundice would last two to three days. During attacks she had pruritus, light stools, and dark urine. She did not lose weight. A diagnosis of choledocholithiasis and stricture of the common duct was made at the clinic in 1952, and operation revealed dilatation of the common duct and stricture of the right and left hepatic ducts. Intrahepaticolithotomy, choledocholithotomy, and double choledochostomy were carried out. A large T-tube was placed in the left hepatic duct and a smaller one in the right hepatic duct. It was planned to leave the T-tubes in for one year. The patient was well for about 15 months. The larger tube became plugged and was partially opened. She returned to the clinic and both tubes were found to be plugged. The larger tube was removed, and four days later the smaller one was removed also.

The intraductal narrowing in this case, of course, may have been the result of the neoplasm, but the history of bile drainage following cholecystectomy and the presence of the common and hepatic duct stones seems to indicate a good chance that the lesion was inflammatory.

I did a double hepaticoduodenostomy for a stricture of the common bile duct on a woman who had had cholecystectomy elsewhere two months previously. After the hepaticoduodenostomies, bile continued to drain from the wound. Three weeks later there was a tender swelling in the right upper quadrant of the abdomen with generalized abdominal tenderness and pain. This was due to an abscess in the abdominal wall, which was drained. Four months later she returned to the clinic because of steady crampy nonradiating pain in the left lower part of the abdomen, with belching and bloating. An indefinite mass was palpable in the right upper quadrant. At exploration diffuse abdominal carcinomatosis was found with multiple regions of incomplete intestinal obstruction. A specimen from the omentum showed scirrhous adenocarcinoma, the origin of which had probably been in the pancreas with extension into the common bile duct, and this was the origin of biliary obstruction.

I have discussed briefly the problems associated with the diagnosis and treatment of malignant lesions of the extrahepatic bile ducts. With the exception of those in and around the ampulla for which surgical removal can be carried out in most cases with relief of jaundice and with prolongation of life, malignant lesions of the bile ducts seldom lend themselves to excision. Temporizing procedures, such as draining the ducts above the obstruction, then, are usually about all that can be offered to the patient. Even these are worth while, since they relieve the jaundice and the intolerable itching that frequently accompanies it.

COMMENT

I should like to express my thanks again for the invitation to present the 25th Arthur Dean Bevan Lecture before you this evening. I was elated when I received your invitation to present a surgical lecture in memory of my first professor of surgery and one of my most interesting teachers, Arthur Dean Bevan, who, with his many brilliant colleagues at Rush Medical College and Presbyterian Hospital, did so much for hundreds of men embarking on careers in medicine and surgery.

REFERENCES

1. Greene, C. H.; Snell, A. M., and Walters, W.: Diseases of the Liver: I. A Survey of Tests for Hepatic Function, Arch. Int. Med. **36**:248 (Aug.) 1925.

2. Rosenthal, S. M.: A New Method of Testing Liver Function with Phenoltetrachlorphthalein: III. Clinical Report, J. A. M. A. **79**:2151 (Dec. 23) 1922.

3. Walters, W.: Pre-Operative Preparation of Patients with Obstructive Jaundice, Surg., Gynec. & Obst. **33**:651 (Dec.) 1921.

4. Mann, F. C., and Magath, T. B.: Studies on the Physiology of the Liver: III. The Effect of Administration of Glucose in the Condition Following Total Extirpation of the Liver, Arch. Int. Med. **30**:171 (Aug.) 1922.

5. Walters, W., and Bowler, J. P.: Pre-Operative Preparation of Patients With Obstructive Jaundice: An Experimental Study of the Toxicity of Intravenous Calcium Chloride Used in the Preparation of Patients, Surg., Gynec. & Obst. **39**:200 (Aug.) 1924.

6. Butt, H. R.; Snell, A. M., and Osterberg, A. E.: The Use of Vitamin K and Bile in Treatment of the Hemorrhagic Diathesis in Cases of Jaundice, Proc. Staff Meet., Mayo Clin. **13**:74 (Feb. 2) 1938.

7. Walters, W., and Bollman, J. L.: Results of Accumulations of Bile Around the Liver: Clinical and Experimental Observations, J. A. M. A. **91**:239 (July 28) 1928.

8. Greene, C. H.; McVicar, C. S.; Rowntree, L. G., and Walters, W.: Disease of the Liver: III. A Comparative Study of Certain Tests for Hepatic Function in Patients with Obstructive Jaundice, Arch. Int. Med. **36**:418 (Sept.) 1925.

9. Greene, C. H.; McVicar, C. S.; Walters, W., and Rowntree, L. G.: Diseases of the Liver: IV. Functional Tests in Cases of Carcinoma of the Liver and Biliary Tract, Arch. Int. Med. **36**:542 (Oct.) 1925.

10. McGowan, J. M.; Butsch, W. L., and Walters, W.: Pressure in the Common Bile Duct of Man: Its Relation to Pain Following Cholecystectomy, J. A. M. A. **106**:2227 (June 27) 1936.

11. McGowan, J. M.; Butsch, W. L., and Walters, W.: The Use of Glyceryl Trinitrate (Nitroglycerin) for the Control of Pain Following Cholecystectomy, Ann. Surg. **104**:1013 (Dec.) 1936.

12. Walters, W., and Parham, D.: Renal and Hepatic Insufficiency in Obstructive Jaundice, Surg., Gynec. & Obst. **35**:605 (Nov.) 1922.

13. Walters, W., and Thiessen, N. W.: Visual Methods of Studying the Physiology of the Common Bile Duct: I. The Problem of Pancreatitis and Sphincteritis, Proc. Staff Meet., Mayo Clin. **9**:772 (Dec. 19) 1934.

14. Swedberg, J.: Routine Cholangiography at Operations for Gall Stones, Acta chir. scandinav. **103**:175, 1952.

15. Lundquist, V. J. P.: Pancreatitis Complicating Common Duct Surgery, Minnesota Med. **36**:167 (Feb.) 1953.

16. Brumm, H. J., and Willius, F. A.: The Surgical Risk in Patients With Coronary Disease, J. A. M. A. **112**:2377 (June 10) 1939.

17. Walters, W., and Kelly, A. H.: Surgical Treatment of Stricture of the Common and Hepatic Bile Ducts: A Twenty-Eight-Year Survey, A. M. A. Arch. Surg. **66**:417 (April) 1953.

18. Walters, W., and Lewis, E. B.: Strictures of the Common and Hepatic Bile Ducts with a Report of Ninety-Eight Cases, in Lahey, F. H.: Frank Howard Lahey Birthday Volume June First, Nineteen Hundred Forty, Springfield, Ill., Charles C Thomas, Publisher, 1940, pp. 443-457.

19. Walters, W.: II. Physiologic Studies in Cases of Stricture of the Common Bile Duct: A 28 Year Survey with Data on 254 Patients, Ann. Surg. **138**:609 (Oct.) 1953.

20. Walters, W., and Marvin, C. P.: Complete Stricture of the Extrahepatic Bile Ducts: External Hepaticostomy Followed by Spontaneous Hepatoduodenal Fistula, Arch. Surg. **57**:18 (July) 1948.

21. Landry, R. M., and Walters, W.: Obscure Malignant Obstructions of the Ampullary Portion of the Common Bile Duct, Proc. Staff Meet., Mayo Clin. **25**:179 (Apr. 12) 1950.

INTESTINAL ANTISEPSIS WITH OXYTETRACYCLINE (TERRAMYCIN) AND NEOMYCIN

A Comparative Study

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IT HAS been of interest during the past two years to compare the effectiveness of oxytetracycline (Terramycin) and neomycin in the preoperative preparation of the colon and rectum.

The late Dr. John Lockwood [1] emphasized that in intestinal surgery chemotherapy of any type was secondary in importance to a good anastomosis on a decompressed bowel with a good blood supply. Poth [2] has shown that there is a much improved quality of healing of large bowel anastomoses performed in dogs after the preoperative use of intestinal antiseptics.

Dearing and Needham [3] and others * have reported on the effect of oxytetracycline on the intestinal bacterial flora of patients, with special reference to the preoperative use of oxytetracyline. Poth and his associates † have reported on the effectiveness of neomycin alone and of neomycin combined with phthalylsulfathiazole in the intestinal antisepsis of patients prior to operation. These studies were conducted on 51 surgical patients with uncomplicated neoplasms of the colon and rectum in order to compare the effectiveness of oxytetracycline and neomycin in various doses.

MATERIALS AND METHODS

Twenty-two patients received oxytetracycline, 500 mg. q. 6 h. for 48 to 54 hours, and seven patients received oxytetracycline, 750 mg. q. 6 h. for 48 to 54 hours. Twenty-two other patients were treated with neomycin; of these, 10 received neomycin 1 gm. q.4.h. for 72 hours, and 12 received neomycin 2 gm. q. 4 h. for 48 hours. One patient received neomycin 2 gm. q. 4 h. for 10 days, owing to the postponement of operation, without ill effects except for slight nausea.

When the decision for operative intervention was made, in addition to the initiation of antibiotic therapy, each patient was given a regimen consisting of (1) a low-residue liquid diet; (2) sodium phosphate, 30 cc. q. d., and (3) enemas twice a day.

Cultures were done on a premedication stool specimen and from a piece of intestinal mucosa from the operative specimen.

Terramycin was supplied by Charles Pfizer & Company, Inc., Brooklyn 6.

Neomycin was supplied by Commercial Solvents Corporation, New York 17.

From the Departments of Surgery and Bacteriology, Duke University School of Medicine.

* References 4 and 5.

† References 6 and 7.

FIG. 1

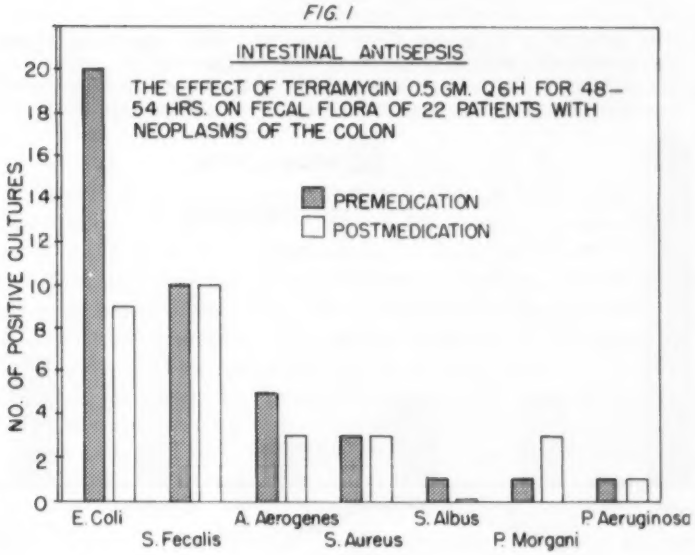

INTESTINAL ANTISEPSIS
THE EFFECT OF TERRAMYCIN 0.5 GM. Q6H FOR 48–54 HRS. ON FECAL FLORA OF 22 PATIENTS WITH NEOPLASMS OF THE COLON
PREMEDICATION
POSTMEDICATION
NO. OF POSITIVE CULTURES
0
2
4
6
8
10
12
14
16
18
20
E. Coli
S. Fecalis
A. Aerogenes
S. Aureus
S. Albus
P. Morgani
P. Aeruginosa

FIG. 2

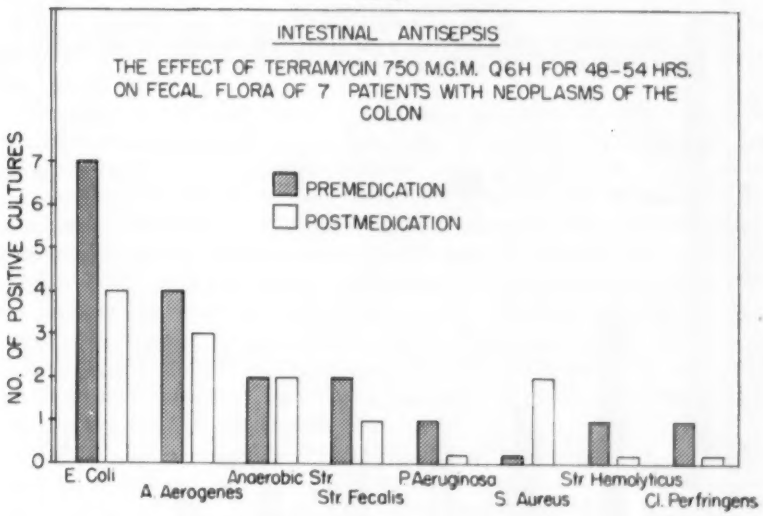

INTESTINAL ANTISEPSIS
THE EFFECT OF TERRAMYCIN 750 M.G.M. Q6H FOR 48–54 HRS. ON FECAL FLORA OF 7 PATIENTS WITH NEOPLASMS OF THE COLON
PREMEDICATION
POSTMEDICATION
NO. OF POSITIVE CULTURES
0
1
2
3
4
5
6
7
E. Coli
A. Aerogenes
Anaerobic Str
Str Fecalis
P Aeruginosa
S. Aureus
Str Hemolyticus
Cl. Perfringens

FIG. 3

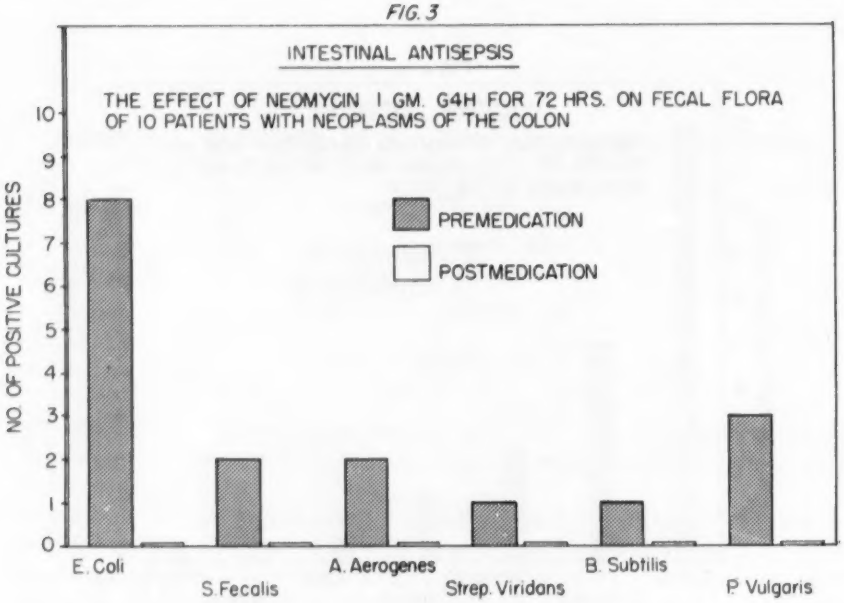
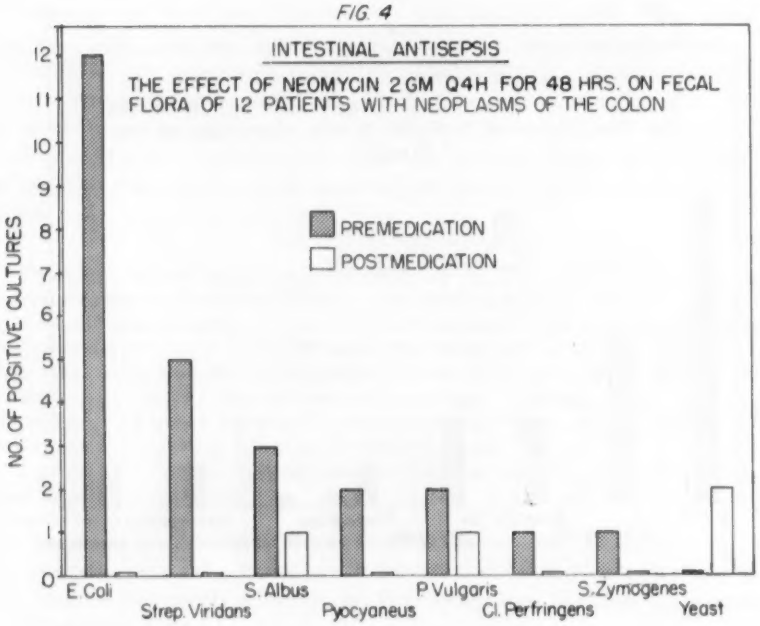

INTESTINAL ANTISEPSIS
THE EFFECT OF NEOMYCIN 1 GM. G4H FOR 72 HRS. ON FECAL FLORA OF 10 PATIENTS WITH NEOPLASMS OF THE COLON
NO. OF POSITIVE CULTURES
PREMEDICATION
POSTMEDICATION
E. Coli
S. Fecalis
A. Aerogenes
Strep. Viridans
B. Subtilis
P. Vulgaris

FIG. 4


INTESTINAL ANTISEPSIS
THE EFFECT OF NEOMYCIN 2 GM Q4H FOR 48 HRS. ON FECAL FLORA OF 12 PATIENTS WITH NEOPLASMS OF THE COLON
NO. OF POSITIVE CULTURES
PREMEDICATION
POSTMEDICATION
E. Coli
Strep. Viridans
S. Albus
Pyocyaneus
P. Vulgaris
Cl. Perfringens
S. Zymogenes
Yeast

A loopful of feces or a piece of mucosa was streaked on the surface of blood agar and eosin-methylene blue agar plates. A tube of thioglycollate medium was also inoculated with the specimen for the growth of anaerobic organisms.

After 24 hours' incubation, the plates were examined, and the different types of colonies were noted. Smears of each type of colony were made and stained by Gram's method. The organisms were identified by the usual methods. A smear was made from the broth culture and also stained by Gram's method. If Gram-positive rods were present in the broth culture, meat and milk media were inoculated for the further identification of the clostridia group of organisms. Anaerobic streptococci were identified by their inability to grow under aerobic conditions.

RESULTS

Oxytetracycline, 0.5 gm. every 6 hours for 48 to 54 hours (Fig. 1), produced a marked decrease in the bacterial count of the intestine; however, there was a persistence of the spectrum of organisms in the majority of cases.

Of 20 patients, 9 still had positive cultures for Escherichia coli. The incidence of positive cultures of Streptococcus faecalis was also unchanged. The incidence and type of positive cultures were not markedly benefitted by increasing the dose of oxytetracycline to 750 mg. every 6 hours for 48 to 54 hours.

In contrast, neomycin 1 gm. every four hours for 72 hours and neomycin 2 gm. every 4 hours for 48 hours produced a drastic reduction in the bacterial count of the intestinal contents and eliminated the majority of the bacteria from the spectrum found preoperatively (Figs. 3 and 4).

The growth of E. coli and streptococcal organisms was totally inhibited by the neomycin; there did not appear to be any advantage in using 2 gm. every four hours over 1 gm. every four hours.

COMMENT

It is of interest that in this study oxytetracycline, 750 mg. every six hours as recommended by Dearing and Needham, was ineffective in reducing the spectrum of the colonic flora.

Neomycin, on the other hand, in doses of 1 gm. every 4 hours for 72 hours, appeared to reduce drastically the colonic flora. The side-effects consisted of frequent loose stools in all 22 cases, nausea without vomiting in 11 cases, and vomiting in 1 case in which the patient received the drug for 10 days. There was no prolongation of the prothrombin time of three patients receiving neomycin, including the patient whose therapy was continued for 10 days. In general, the side-effects of neomycin, 1 gm. every four hours, were similar to those of oxytetracycline, 750 mg. every six hours, as judged by the various members of the surgical staff.

Neomycin appears to approach closely the properties of the ideal intestinal antiseptic listed by Poth, i. e., low toxicity, broad bacterial spectrum, rapid activity, permits adequate food and fluid intake, and aids in mechanical cleansing of the bowel without causing dehydration.

In these studies, neomycin 1 gm. every four hours appeared to inhibit the growth of Aerobacter aerogenes, and therefore it was not deemed necessary to combine neomycin with a sulfonamide. Open anastomosis of the large bowel may therefore be carried out safely with minimal risk of seeding the peritoneal cavity with bacteria present in the usual large intestine. Neomycin is currently the intestinal antiseptic of choice in this hospital in the preoperative preparation of the large bowel.

CONCLUSIONS

1. Oxytetracycline (Terramycin) in doses up to 750 mg. every 6 hours for 48 hours appears to reduce the intestinal bacterial count without any marked change in the floral spectrum.

2. Neomycin in doses of 1 gm. every 6 hours for 72 hours or 2 gm. every 4 hours for 48 hours appears to inhibit the growth of almost all bacterial flora of the intestine; it appears to be a safe and satisfactory drug in the preoperative antisepsis of the colon and rectum.

3. Neomycin is currently the drug of choice for intestinal antisepsis. The bacterial inhibition is more complete than with oxytetracycline; the side-effects of the drug are essentially similar to those produced by oxytetracycline.

REFERENCES

1. Lockwood, J.: Letter to the Editor, Ann. Surg. **132**:319, 1950.

2. Poth, E. J.; McNeil J. P.; Manhoff, L. J.; King, W. B., and Sinclair, J. G.: The Healing of Bowel as Influenced by Sulfasuxidine and Sulfathalidine, Surg., Gynec. & Obst. **86**:641, 1948.

3. Dearing, W. H., and Needham, Gerald M.: The Effect of Terramycin on the Intestinal Bacterial Flora of Patients Being Prepared for Intestinal Surgery, Proc. Staff Meet., Mayo Clin. **26**:49, 1951.

4. Herrell, W. E.; Heilman, F. R.; Wellman, W. E., and Bartholomew, L. G.: Terramycin: Some Pharmacologic and Clinical Observations, Proc. Staff Meet., Mayo Clin. **25**:183, 1950.

5. Di Caprio, J. M., and Rautz, L. A.: Effects of Terramycin on the Bacterial Flora of the Bowel in Man, Arch. Int. Med. **86**:649, 1950.

6. Poth, E. J.; Fromm, S. M.; Wise R. I., and Hsiang, C. M.: Neomycin, a New Intestinal Antiseptic, Texas Rep. Biol. & Med. **8**:353, 1950.

7. Poth, E. J.; Fromm, S. M.; Martin, R. G., and Hsiang, C. M.: Neomycin: An Adjunct in Abdominal Surgery, South, J. J. **44**:226, 1951.

CLINICAL TRIALS OF A NEW PLASTIC DRESSING FOR BURNS AND SURGICAL WOUNDS

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DAYTON, O.

IN A PREVIOUS paper,[1] Choy and Wendt reported the development of a rapidly sprayable, transparent, film-forming polyvinyl plastic dressing * for the mass therapy of burns in disaster situations such as atomic blast.

Among the advantages which made it particularly suited for the mass therapy of burns when it was dispensed from an aerosol bomb were (1) a marked saving of time over conventional pressure dressings in application (Fig. 1); (2) the feasibility of its use by relatively untrained personnel; (3) applicability to parts of the body poorly adapted to pressure dressings; (4) transparency, allowing frequent inspection of the burned area without removal of the dressing; (5) flexibility, allowing relatively unrestricted early exercise of burned hands and digits without loss of integrity of the dressing; (6) impermeability to bacteria; (7) minimal

TABLE 1.—*Results of Patch Tests with Aeroplast on 1,052*

Reactions	After 24 Hr.	After 48 Hr.
0	1,047	1,049
±	4	2
+	1	1
% of positive reactions *	0.48	0.29

* Including ± reactions.

storage problems, including the elimination of the necessity for periodic resterilization; (8) moderate bacteriostasis (Fig. 2); (9) the absence of tourniquet effect on limbs and restriction of respiration when applied to the abdomen or thorax, and (10) portability and feasibility of use under adverse conditions in the field.

In preliminary experiments with animals and human beings, it was found that experimental burns healed successfully under the plastic (Aeroplast) dressing; there was no systemic or local toxicity,[1] and there was no evidence of sensitivity

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* Aeroplast is prepared by the Aeroplast Corporation, 420 Dellrose Ave., Dayton, O., under the trade name "Aeroplast," and is available through standard pharmaceutical channels as an ethical product. Composition: Aeroplast contains copolymers of hydroxyvinyl chloride-acetate and sebacic acid, 9.3% by weight, and modified maleic rosin ester, 3.1% by weight, in an ethyl acetate-acetone solvent, with a fluoro-chloro hydrocarbon as a gaseous propellant. Aeroplast has been approved by the United States Food and Drug Administration.

(Table 1). Comparative wound healing studies revealed no difference in healing rates between wounds dressed with Aeroplast and control wounds dressed with petrolatum (Vaseline) gauze.[2]

METHODS

Clinical trials of the Aeroplast were conducted on The Third Surgical Division, Bellevue Hospital,† New York.

All wounds were treated in accordance with usual surgical practice. The Aeroplast was then applied by either (*a*) spraying from an aerosol bomb or a spray gun operated by a portable

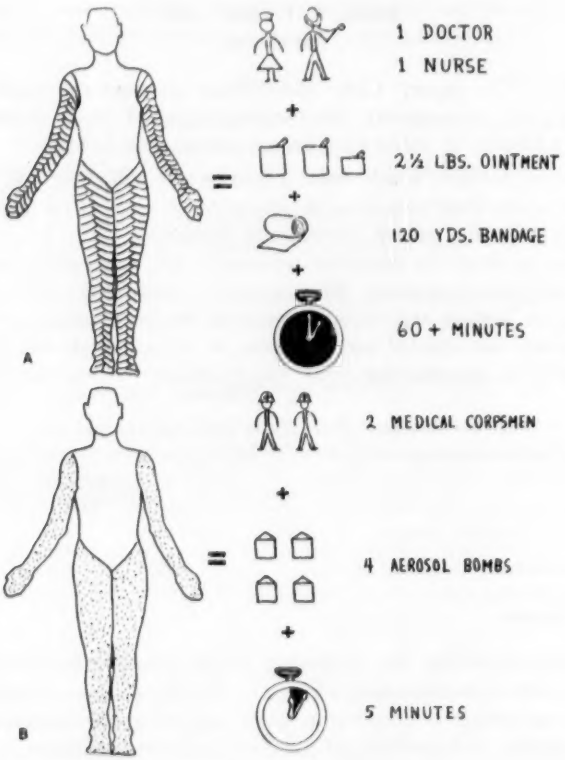

Fig. 1.—Comparison of treatment of 50% body burn by *A*, standard pressure bandage and *B*, plastic-spray dressing. (Data was derived from tests on mannikins.) (Reprinted with permission from the United States Armed Forces Medical Journal.)

air compressor, or (*b*) direct painting onto the lesion with a 2 by 2 in. piece of gauze on straight forceps or an applicator stick. In all cases, a one to two inch margin of normal skin was included in the dressing. Color photographs were taken before and after application of the dressing and serially during wound healing. Clinical observations were made daily, and the Aeroplast dressing changed as necessary by simply peeling it off as a sheet and reapplying.

† Under the sponsorship and direction of Dr. John Mulholland, Chief, The Third Surgical Division, Bellevue Hospital, New York.

Fig. 2.—Agar plates, *A*, streaked with Staphylococcus aureus; *B*, seeded with Pseudomonas aeruginosa; *C*, seeded with an aerobic spore former and Proteus vulgaris. Plastic film was sprayed on top half of plate *A* within two hours and on plates *B* and *C* after 24 hours incubation. Note inhibition of growth on top half of all plates 24 hours later. (Reprinted with permission from the United States Armed Forces Medical Journal.)

Serial liver profile, renal function, and hematological studies were contemplated to further confirm the results of previous animal experiments demonstrating the nontoxicity of the Aeroplast dressing. These, however, were soon abandoned because of the prevalence in our series of patients of acute alcoholism, Laennec's cirrhosis, malnutrition and pulmonary tuberculosis.

It was decided to include a wide variety of surgical wounds other than burns in order to determine the precise areas of efficacy and the limitations of the Aeroplast.

RESULTS

A total of 50 patients were treated; of these 11 had burns, from first to third degree; 8 had skin graft donor sites, which were regarded as second degree burn equivalents, and 31 had other types of surgical lesions, including operative wounds, lacerations of hands, neck, face and scalp, open reductions of fractures, decubiti, granulating wounds and colostomies.

TABLE 2.—*Skin Graft Donor Sites*

Case No.	Sex	Age	Primary Diagnosis	Healing Time (Days)	Infection
1	M	27	Third degree burn	18	No
2	M	65	Stasis ulcers, left leg	13	No
3	M	42	Stasis ulcers, right leg pulmonary tuberculosis, active; chronic alcoholism	10 after Aeroplast; incomplete healing, 76 days prior to Aeroplast	No
4	M	57	Gangrene, right buttock and scrotum; malnutrition; severe chronic alcoholism	9	No
5	M	50	Paraplegia; skin defect, left foot, secondary to extravasated infusion	12	No
6	M	49	Third degree burn; Korsakoff's psychosis	8	No
7	M	65	Chronic alcoholism; traumatic ulceration, left leg	7	No
8	M	59	Malnutrition stasis ulcers, left leg	9	No

SKIN GRAFT DONOR SITES

Of the eight skin graft donor sites treated, all healed without infection in an average of 11 days (Table 2).

Because of fluid collection underneath the dressing, in Case 1, E. J. (Fig. 3), two changes of dressing were required, and in Cases 2, F. F., and 3, W. H., one change of dressing each was required. The remaining five skin graft donor sites reepithelized under the single, original dressing.

CASE 3.—W. H. was a chronic alcoholic with active pulmonary tuberculosis and stasis ulcers of the right lower leg. A split-thickness skin graft was taken from the inner aspect of the left thigh. After 76 days, the donor site, treated first with petrolatum gauze and subsequently with the open air exposure method, was approximately 70% nonepithelized because of repeated infection with Pseudomonas aeruginosa and breakdown of the new epithelium. The Aeroplast dressing was then tried, successfully, with complete epithelization 10 days later.

BURNS

Of the 11 burns treated, five were infected with P. aeruginosa; of these, three were infected prior to and two were infected subsequent to the application of Aeroplast. Two patients were lost to follow-up examination. The three outstanding observations made were (1) the Aeroplast could be applied very quickly;

(2) in first and second degree burns there was pronounced subjective relief of pain (after the initial sharp "stinging" sensation wore off with evaporation of the ethyl acetate solvent; this usually lasted 30 to 45 seconds), and (3) the transparency of the Aeroplast permitted early detection of infection.

CASE 1.—The patient, E. J., was a 22-year-old Negro man admitted July 4, 1952, for first, second and third degree burns of the right thigh and leg sustained when a fire rocket entered his trouser leg. The first and second degree burns healed in four to seven days with open air exposure. The third degree burn measuring 9 by 8 cm. was grafted on July 30. There was an incomplete take (approximately 75%), with a superimposed P. aeruginosa infection under the pressure dressing. The lesion was exposed for 24 hours before he was first seen by me. The Aeroplast dressing was applied on August 7 and changed once on August 8 because of moderate fluid accumulation underneath. The P. aeruginosa infection subsided, no other dressings were required, and the burn epithelized completely on August 18.

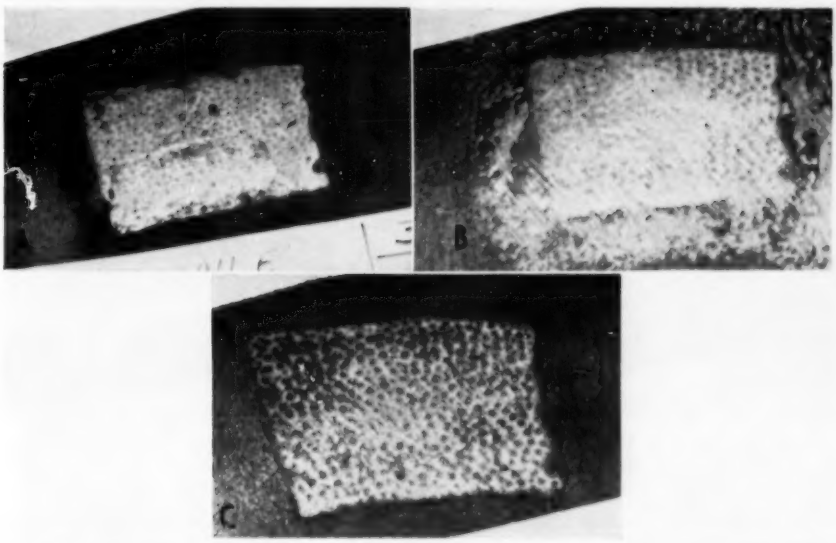

Fig. 3 (Case 1, E. J.).—*A*, skin graft donor site, seven days after operation. *B*, skin graft donor site with aeroplast dressing, 14 days after operation. Note partial return of pigmentation visible through transparent dressing. *C*, skin graft donor site, healed, 18 days after operation.

CASE 2.—The patient, C. B., was a 24-year-old Negro man admitted Aug. 21, 1952, for a second degree friction burn of the entire dorsal surface of the left forearm, sustained in an automobile accident (Fig. 4). He first received surgical attention 12 hours after the injury, at which time the burn was débrided and dressed with petrolatum gauze. This was removed on August 22 and Aeroplast applied. Between this time and September 2 the dressing was changed twice because of a low-grade P. aeruginosa infection. On September 2, there was no further evidence of infection, and evidence of healing appeared with the return of pigmentation in scattered areas. The burn was completely epithelized by Sept. 8, 1952.

CASE 3.—The patient, C. B., was a 31-year-old white man admitted Aug. 23, 1952, for second degree circumferential burns of the digits and dorsum of both hands and second and third degree burns of the entire left lower leg except for the plantar surface of the foot, sustained in a gasoline fire. The Aeroplast dressing was applied with marked subjective relief from pain. The patient was encouraged to use his hands, and did so so vigorously that the dressing over the

finger pads and web spaces had to be "mended" daily by being painted over with plastic as breaks developed. On the third hospital day, the blisters over the fingers, hands and left foot and ankle were excised and the Aeroplast reapplied. A second change of dressing was done on August 29. On Sept. 2, 1952, both hands were completely epithelized with full function. However, the burn on the leg became infected with P. aeruginosa, the Aeroplast was removed, and the burn successively treated with acetic acid soaks, open exposure, antibiotics and physiotherapy. On September 29, the burn had healed sufficiently to warrant discharge of the patient.

CASE 4.—The patient, E. W., was a 54-year-old white man admitted August 15, with a diagnosis of active pulmonary tuberculosis and a 3 by 4 cm. third degree burn of the right ankle, sustained on Aug. 1, 1952. On application of nitrofurazone (Furacin) and saline dressings, the burn became grossly infected with P. aeruginosa. Application of Aeroplast dressings was started on August 25. Until September 4, the Aeroplast was changed every 2 to 3 days with soap, peroxide and saline preparation. The P. aeruginosa infection remained stationary; new epithelium 0.5 to 1.0 cm. wide grew in from the margins, and there were healthy granulations. On September 4, it was decided to change to acetic acid soaks. By September 9, the lesion was completely epithelized.

CASE 5.—The patient, J. H., was a 41-year-old Negro man admitted Aug. 12, 1952, for first and second degree flash burns of the face, neck, upper trunk, volar surfaces of both arms, right forearm and right palm, sustained while tending a furnace. Ninety per cent of the burned area consisted of first degree burns. All the burns, except those on the face, were sprayed with Aeroplast. There was almost immediate subjective relief of pain in the sprayed areas; the burns

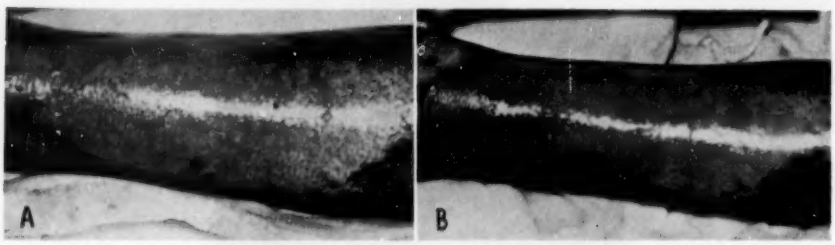

Fig. 4 (Case 2, C. B.).—*A*, second degree burn, dorsum of left forearm. *B*, second degree burn with Aeroplast dressing.

on the face remained painful. The first degree burns were asymptomatic at the end of 24 hours. The second degree burns were completely epithelized by August 18, there having been no difference in healing time between those treated with exposure and those treated with Aeroplast.

CASE 6.—The patient, M. W., was a 29-year-old Negro man admitted from another hospital Sept. 2, 1952, to the prison ward for a deep laceration involving the joint capsule and a deep second degree friction burn of the left shoulder measuring 14 by 17 cm. and two second degree friction burns of the left wrist and dorsal surface of the left forearm measuring 10 by 4 cm. and 15 by 6 cm. respectively. These injuries were sustained in a stolen truck on August 30. The patient was first seen by us on September 3, four days after the injury, at which time the shoulder lesion was clean and the forearm lesions were grossly infected with P. aeruginosa. The petrolatum gauze dressings were replaced with Aeroplast; this was changed every three days. On September 11, the patient was transferred to prison. At this time the P. aeruginosa infection of the forearm lesions had neither improved nor progressed; the shoulder lesion was 50% healed, with zones of reepithelization 1.0 to 4.0 cm. wide.

CASE 7.—The patient, G. D., was a 38-year-old white waitress first seen in the outpatient department Sept. 11, 1952, with circular second degree burns on all fingers and the dorsum of the left hand, sustained through immersion in boiling water (Fig. 5). Aeroplast was applied within 30 minutes with no débridement, the blisters were excised on the third day and Aeroplast

was reapplied. The patient was given a small supply of Aeroplast and instructed to "touch up" any cracks that developed. She was seen every other day, and at no time was there evidence of infection. The Aeroplast was changed again on September 19. On September 23, there was complete healing with full function. Throughout this period she continued working as a waitress, using her injured hand, although she was advised to keep the hand protected.

Case 8.—The patient, B. S., was a 36-year-old white man admitted Sept. 12, 1952, with a first, second and third degree burn involving the posterior surface of the distal half of the left arm, the elbow, and the left forearm. This was sustained in a freak accident in which the patient was waiting for a traffic light with his arm on the window sill of his car when a gas explosion occurred in an open man hole. Aeroplast was applied with dramatic relief of pain. On the second hospital day, however, the patient signed out to seek private care.

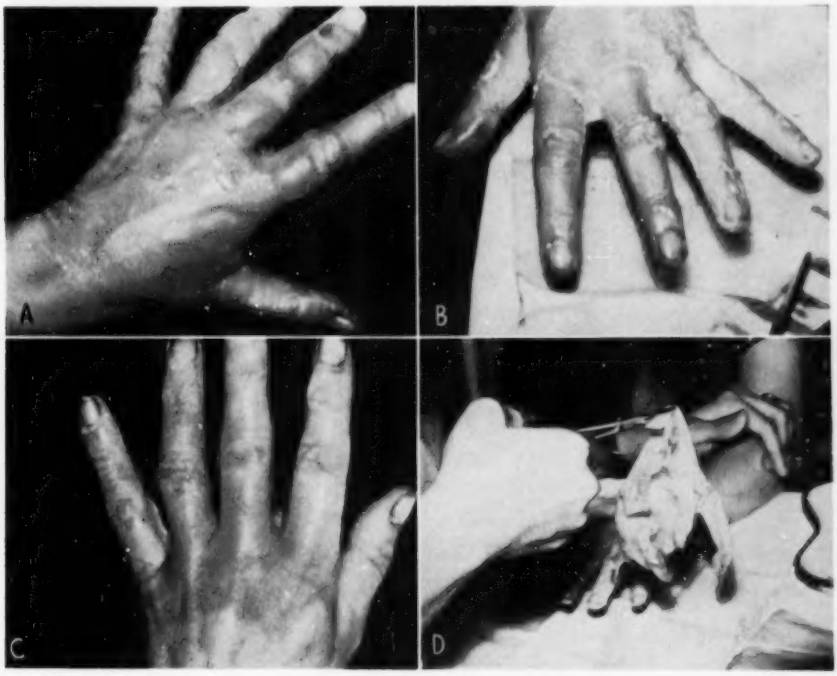

Fig. 5 (Case 7, G. D.).—*A*, second degree burn of left hand with Aeroplast dressing. Note blister formation. *B*, same burn after excision of blisters and application of Aeroplast. *C*, same burn with complete reepithelization 12 days after burn. *D*, note removal of Aeroplast dressing as an entire "Glove."

Case 9.—The patient, M. B., was a 42-year-old white man seen in the OPD Sept. 17, 1952, with first degree flash burns of the posterior aspect of the neck and both shoulders (a vest distribution) sustained in a rubber cement fire. The patient complained bitterly of pain until the Aeroplast was applied. The patient was instructed to return the following day but failed to do so.

Case 10.—The patient, G. A., was an 11-year-old girl first seen in the out patient department, Sept. 24, 1952, with second degree burns of the dorsal aspects of the third, fourth and fifth fingers of the right hand, sustained four days previously in a frying-pan fire. When she was seen, the blisters had ruptured, and Aeroplast was applied without débridement. On September 25, the blisters were excised, and Aeroplast was reapplied. No other dressings were required and healing was complete, without infection by Oct. 1, 1952.

TABLE 3.—*Surgical Wounds Treated with Aeroplast*

Wound	Number
Appendectomy	4
Laparotomy	2
Cholecystectomy	2
Herniorrhaphy	5
Open reduction of fracture	3
Kirschner wire fixation	2
Incision and drainage of abscess	2
Laceration	4
Ulcer, skin	3
Gastrostomy and ileostomy	2
Saphenous vein ligation	1
Stasis dermatitis	1
Total	31

TABLE 4.—*Results of Surgical Lesions Treated with Aeroplast*

Case No.	Sex	Age	Primary Wound	Healing Time (Days)	Infection
1	M	20	Appendectomy	7	No
2	M	20	Appendectomy	6	No
3	M	34	Appendectomy	9	No
4	F	20	Appendectomy; pregnancy, 5 mo.	6	No
5	M	63	Exploratory laparotomy	10	No
6	M	61	Exploratory laparotomy	8	No
7	M	43	Cholecystectomy	7	No
8	F	31	Cholecystectomy	13	No
9	M	69	Herniorrhaphy, bilateral	8	No
10	M	48	Herniorrhaphy, bilateral	Right 7; left dehisced on first postoperative day	No
11	M	64	Herniorrhaphy	17	Yes
12	M	38	Herniorrhaphy	6	No
13	M	80	Herniorrhaphy	13	No
14	F	77	Smith-Petersen intramedullary nailing of hip	9	No
15	F	32	Open reduction, left femur	5	No
16	F	35	Open reduction, left radius and ulna	11	No
17	F	34	I & D of large abscesses, both buttocks	11	No
18	M	65	I & D of carbuncle, left temporal scalp, required stamp graft	11	No
19	M	32	Laceration, left hand	9	No
20	F	34	Laceration, left hand	6	No
21	M	43	Laceration, neck, 15 cm. long	4	No
22	M	67	Laceration, face, 10 cm. long	4	No
23	F	70	Decubitus ulcer, 7 × 5 cm.	2 × 1 cm. in 30 days	No
24	M	31	Traumatic ulcer, left foot, 7 × 3 cm.	16	No
25	M	42	Stasis ulcer, right heel, 20 × 15 cm.	No healing	...
26	F	65	Stasis dermatitis, both lower legs	No healing	...
27	M	32	Excoriated abdomen from ileostomy	1	No
28	M	25	Excoriated abdomen from gastrostomy	1	No
29	F	45	Bilateral saphenous vein ligation	5	No
30	M	65	Kirschner wire fixation, supracondylar fracture, right femur	..	No
31	M	34	Kirschner wire fixation, transverse fracture, right tibia and fibula	..	No

CASE 11.—The patient, A. B., was a 22-year-old white nurse who sustained first and second degree burns of the dorsal aspects of the third and fourth fingers, and the distal half of the dorsum of the left hand. Aeroplast was applied, with relief of pain. No change of dressing was required, and complete healing occurred five days later.

OTHER SURGICAL WOUNDS

The Aeroplast dressing was successfully used on a wide variety of surgical wounds (Table 3). The results of treatment are summarized in Table 4. In most cases, one dressing applied in the operating room was sufficient until the sutures were removed. The advantages of the window effect of transparency, and the

Fig. 6 (Case 22, F. L.).—Laceration of face with Aeroplast dressing.

elimination of dressing changes in most of these cases, proved not unacceptable to the hard working staff. The Aeroplast was excellent for lacerations of the scalp, face (Fig. 6), neck and hands, areas which are poorly suited to gauze and adhesive tape dressings. Perhaps the most dramatic application of the Aeroplast was its use on an abdominal wall markedly excoriated by an ileostomy (Case 27, L. S.); there was almost immediate subjective relief of discomfort, and 24 hours later there was an 80% clearing of the excoriations (Fig. 7). It was used with moderate success on one decubitus ulcer (Case 23, N. C.) and with marked success on a traumatic ulcer (Case 24, A. W.) (Fig. 8). Its use on open reductions of fractures made feasible the application of skintight plaster casts, since the bulk of the usual gauze dressings was eliminated. The sites of emergence of Kirschner wires from skin are often subject to low-grade infections. The use of Aeroplast in

two cases (Cases 30, H. M., and 31, J. W.) sealed off these areas effectively for three and four weeks respectively. The absence of infection in these two cases must be attributed at least in part to the Aeroplast. One wound infection (Case 11, L. B.) was encountered. Four cases warrant comment.

CASE 11.—The patient, L. B., was a 64-year-old white man with an indirect left inguinal hernia. A herniorrhaphy performed on Sept. 3, 1952, was dressed with Aeroplast on the first postoperative day. On the fifth postoperative day, the wound was observed to be infected and 5 to 7 cc. of dark red blood was aspirated from the inferior end of the wound. The Aeroplast

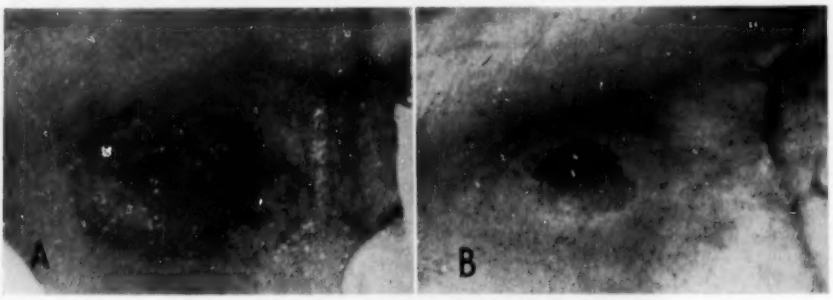

Fig. 7 (Case 27, L. S.).—*A*, ileostomy with excoriated surrounding skin. *B*, ileostomy, 24 hours after application of Aeroplast.

Fig. 8 (Case 24, A. W.).—Traumatic ulcer treated with Aeroplast. Complete epithelization 16 days posttrauma.

was replaced with a gauze dressing and administration of antibiotics begun. The wound healed completely on the seventeenth postoperative day after the infection gradually subsided.

CASE 25.—The patient, W. H., was a 42-year-old white man with a large stasis ulcer of the right heel measuring 20 by 15 cm. Concurrent diagnoses were pulmonary tuberculosis, active; chronic alcoholism; Laennec's cirrhosis, and malnutrition. After a skin graft failed to take, the Aeroplast dressing was applied on September 26, 1952. After 10 days, it was obvious there was no progression of healing. The use of Aeroplast was therefore discontinued.

CASE 26.—The patient, A. C., was a 65-year-old white woman with diabetes and a severe weeping stasis dermatitis of both lower legs. It was decided to attempt to prevent a breakdown of the skin by protecting the legs with Aeroplast. The use of Aeroplast was discontinued after two days because of excessive accumulation of fluid underneath the dressing.

CASE 29.—The patient, M. G., was a 45-year-old white woman with the diagnoses of psychosis, manic-depressive type; obesity, severe, and varicose veins. A bilateral saphenous vein ligation was performed on Sept. 4, 1952. Postoperatively the wounds were macerated by (1) a pendulous abdomen and pubic hairs abrading the upper thighs and (2) urinary incontinence. On the second postoperative day, the macerated wounds were treated with Aeroplast to exclude the urine. Gauze and adhesive plaster were applied over the Aeroplast to protect the plastic dressing against mechanical trauma from the pendulous abdomen. Under this regimen, the wounds healed in five days, and the macerated areas gradually returned to normal after 12 days.

COMMENT

The Aeroplast, originally designed as an emergency, initial local dressing for the mass treatment of thermal burns pending (1) the mobilization of existing medical resources and (2) the evacuation of these burn casualties to centers for definitive therapy, must, in the light of clinical trials described in the foregoing material, be regarded as a new type of general surgical dressing with certain advantages and certain limitations. The evidence indicates that the essentials of a good surgical dressing are met: (1) no retardation of wound healing, (2) ability to maintain the sterility of a clean wound, (3) ease of application and removal, (4) transparency.

The chief drawback of the Aeroplast proved to be the 30 to 45-second period of sharp stinging felt when the dressing was applied to a raw area. The stinging sensation was of the order of magnitude of the burning caused by sodium ethylmercurithiosalicylate (Merthiolate) or alcohol. It was felt that the following considerations tend to minimize the importance of this undesirable characteristic: 1. The Aeroplast does not cause stinging in first and third degree burns or in granulating wounds. 2. The burning sensation lasts only 30 to 45 seconds and is no worse than that caused by standard antiseptics such as sodium ethylmercurithiosalicylate and alcohol. 3. All surgical wounds can be dressed while the patient is still under anesthetic. 4. The problem of burning is trivial in relation to the time and personnel saving advantages of the Aeroplast in the treatment of burn casualties of disaster proportions.

Use of the Aeroplast as an initial temporary dressing to prevent further wound contamination opens channels of use in front line battalion aid stations, in bomber aircraft on extended missions over hostile territory, in airfield crash ambulances and in military and civilian rescue operations following atomic attack.

Use of the Aeroplast as a definitive dressing for surgical wounds affords the advantages previously described.

SUMMARY

A discussion of a new type of general surgical dressing (Aeroplast), utilizing a modified polyvinyl plastic dispensed from an aerosol bomb, is presented.

The results of two months of clinical trials with the Aeroplast are presented.

The advantages and limitations and the possible uses of the Aeroplast dressing are discussed.

Help was given by the House Staff and Technical Sergeant James Edwards, United States Air Force, was of invaluable assistance.

REFERENCES

1. Choy, D. S. J., and Wendt, W. E.: A New Local Treatment of Burns, U. S. Armed Forces M. J. **3**:1241-1255 (Sept.) 1952.

2. Choy, D. S. J.: Comparative Wound Healing Rates of Standard and Experimental Burn Dressing, Armed Forces M. J., to be published.

TREATMENT OF SURGICAL SHOCK WITH ARTERENOL

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OF ALL the objective criteria of the status of a patient in shock, the level of the arterial blood pressure is by far the most commonly used in estimating the clinical state and prognosis. This is reasonable, since the level of arterial tension is one of the major factors in the delivery of nutrient blood to the various organ systems. Hypotension of sufficient severity and duration is fatal. Thus all measures which will restore the blood pressure to normal have potential therapeutic usefulness. In most instances of surgical shock the restoration of fluid volume by use of electrolytes, plasma, blood, or colloids is adequate for the correction of the shock state. However, there is a significant group of patients in whom the response to infusion is slow in appearing or does not appear at all. Additional methods of treatment are necessary in this group and the most logical of these is the use of pressor drugs.

Although this principle is obvious, most of the standard works on surgery and shock dismiss the use of pressor drugs with a few lines about their ineffectiveness. Our interest in this problem was occasioned by two events.

The first was a report by Goldenberg and his associates [1] describing the physiologic action of *l*-arterenol (*l*-nor-epinephrine, Levophed) in man. This group showed that *l*-arterenol causes a rise in blood pressure, both systolic and diastolic, by effecting an over-all increase in peripheral resistance without any direct cardiodynamic action. Epinephrine, on the other hand, causes an increase of the systolic blood pressure mainly by stimulating the heart rate and the strength of systolic ejection. It causes a slight drop of the diastolic blood pressure and an over-all diminution of the peripheral resistance. In addition, these authors showed that the action of *l*-arterenol is short-lived and easily controlled when the drug is used in constant intravenous infusion. It would seem that this drug has many characteristics desirable for the treatment of hypotension, and in a later publication Goldenberg and his associates [2] described its use in combating the hypotension associated with sympathectomy and mentioned its use also in a few instances of hemorrhagic shock.

From the Medical and Surgical Services of Halloran and Brooklyn Veterans Administration Hospitals.

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The second event was our experience in treating an aged patient with a perforated gastric ulcer. This case has been reported in detail elsewhere,[3] but because of its importance it will be reviewed briefly here.

F. F., a 73-year-old white man, was admitted to the hospital with a four-day history of epigastric distress which had become increasingly severe 24 hours previously (Fig. 1). The patient was in profound shock, with absent pulse and blood pressure, cold clammy skin, slight cyanosis, and poorly audible heart sounds. His abdomen was tympanitic, and fluid was present. X-ray studies showed free air in the peritoneal space. A diagnosis of perforated viscus was established, but the surgeons felt that intervention would be fatal because of the patient's poor condition.

Antishock therapy consisting of 500 cc. of whole blood, 500 cc. of plasma, 1,000 cc. of 5% dextrose in saline, and 200 cc. of dextrose in distilled water did not appreciably affect his general state, and *l*-arterenol* was then administered. The response was prompt and dramatic Operation was performed, and the patient made an uneventful recovery.

This case speaks for itself. The patient appeared doomed prior to treatment. The amount of blood and plasma given may have been inadequate to combat the

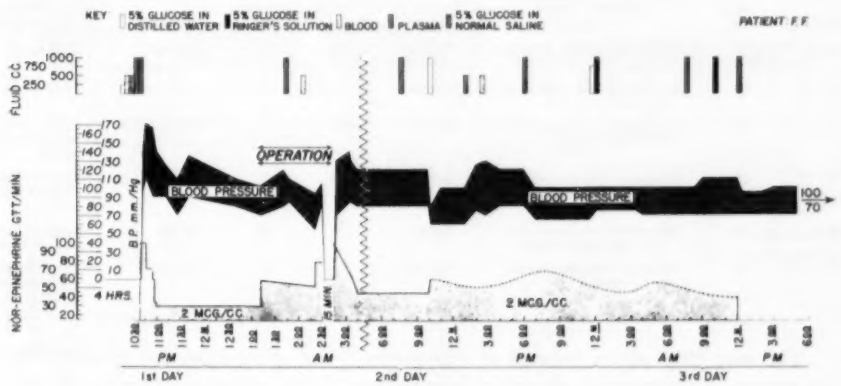

Chart 1.

shock, but because of the patient's age and unknown cardiovascular status we were fearful of overtransfusing. Nevertheless, without any further transfusion of blood or plasma, *l*-arterenol sufficed to bring him out of shock. Whenever the drug was discontinued, his blood pressure dropped sharply and the signs of shock reappeared. In other words, fluid replacement which in itself was inadequate became adequate with *l*-arterenol. It enabled the surgeons to perform a needed operation that would have been otherwise impossible.

Because of the dramatic response of this case, we decided to investigate further the usefulness of this drug in the treatment of shock of different etiologies. Thus far, we have given treatment in 22 cases of surgical and in 10 cases of neurological interest, the latter to be reported separately.[4] The groups reported here consist of six cases of shock associated with an acute surgical abdominal condition, 12 cases

* Generous supplies of *l*-arterenol (Levophed) were obtained through the courtesy of Winthrop-Stearns, Inc., New York 18.

of shock occurring during or after major operative procedures and associated in 3 instances with considerable blood loss, and, finally, 4 cases of severe hemorrhagic shock.

I. SHOCK ASSOCIATED WITH ACUTE SURGICAL ABDOMINAL CONDITIONS

The group of patients belonging to this category present a type of shock that defies simple classification on the basis of pathogenesis. Multiple factors appear to be responsible,[5] i. e., widespread vasodilation and possible cardiac damage as a result of the toxemia and infection and some reduction of the blood and plasma volume. These cases were therefore grouped according to the clinical picture (Table 1).

TABLE 1.—*Data on the Use of Arterenol in Six Patients with Shock Associated with Acute Surgical Abdomen*

Patient	Age, Yr.	Primary Cause of Shock	Degree of Shock	Primary Cause of Shock Removed	Duration of Arterenol Infusion, Hr.	Outcome	Type of Surgical Treatment
F. F.	73	Perforation of gastric ulcer	Severe	Yes	37	Recovery	Definitive
J. W.	58	Strangulating volvulus of colon	Severe	Yes	48	Recovery	Definitive
W. A. I.	48	Perforation of appendix with peritonitis	Severe	No	13	Temporary recovery	None; died 4 days later in coma
W. H.	72	Esophagoperitoneal fistula with peritonitis and mediastinitis	Severe	No	26	Death	Exploratory laparatomy
S. G.	53	Mesenteric thrombosis with paralytic ileus	Severe	No	20	Death	Exploratory laparatomy
C. W. W.	50	Multiple small bowel perforation	Severe	No	10	Death	None; primary cause unrecognized

The case cited above belongs in this group. Four other cases are appended to this report. A sixth case is described here because of the light it shed on the mechanism of the treatment.

J. W., a 58-year-old emaciated white man with far-advanced rheumatoid arthritis of long duration and chronic osteomyelitis, complained of abdominal pain early in the morning of July 21, 1950. A diagnosis of a strangulating lesion of the bowel was made, but surgery could not be performed because he was in deep shock. Blood pressure and pulse were unobtainable; heart tones were hardly audible, and the heart rate as determined by electrocardiograms was 160 beats a minute. His skin was cold and wet. Administration of *l*-arterenol was started and this was combined with blood transfusion. Sufficient improvement took place so that operation was now possible. A large volvulus of the cecum, ascending and proximal half of the transverse colon was found, and this whole segment of gangrenous bowel was resected. His condition improved after surgery, and after 40 hours the *l*-arterenol was discontinued.

Large quantities of *l*-arterenol at first gave a measurable response (Chart 2), but it was far from satisfactory. *l*-Arterenol was then combined with rapid transfusion and a better response was obtained. That this was not due to the transfusion alone was shown by the fall in blood pressure when the drug was discontinued. When the *l*-arterenol was administered again, the pressure rose and was maintained at a good level. Despite the second transfusion the blood pressure fell again when *l*-arterenol was discontinued. Thereafter, both blood and *l*-arterenol were used concurrently, and the patient had so improved that an extensive operation was successfully performed.

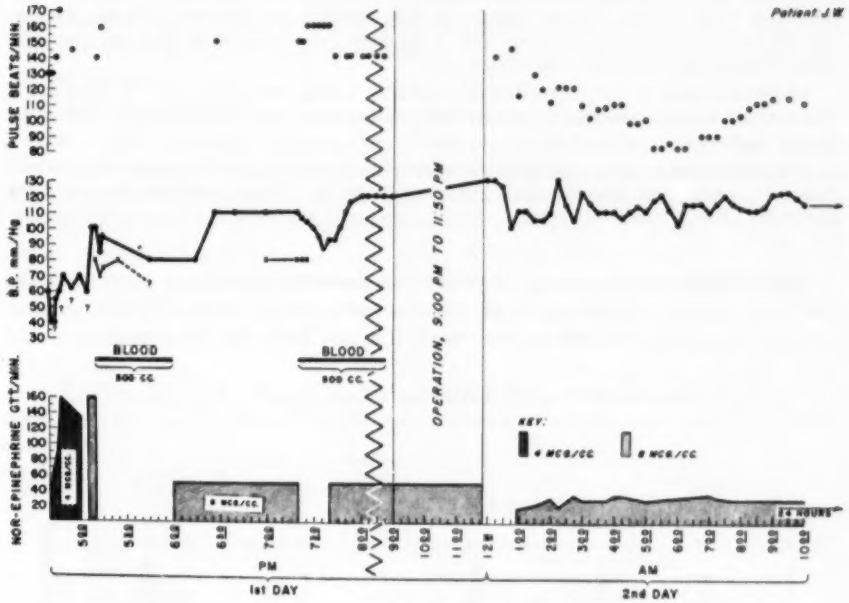

Chart 2.

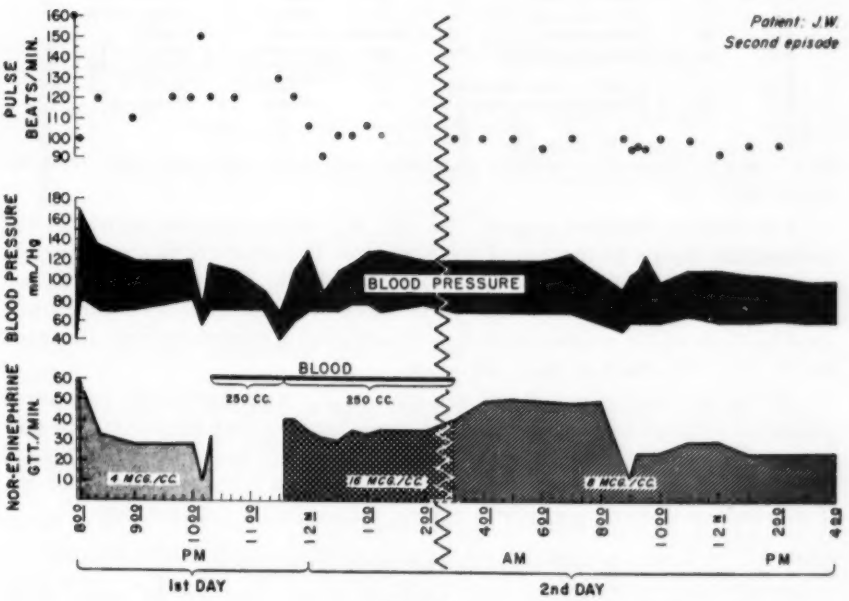

Chart 3.

In all probability *l*-arterenol was not very effective at first because of great diminution in the circulating blood volume. A large quantity of fluid, probably not less than 2,000 ml., was lost into the lumen and into the edematous wall of the destroyed bowel. When fluid was given, the patient became more responsive to *l*-arterenol.

l-Arterenol causes a rise in intra-arterial tension by causing vasoconstriction. In doing this it contracts the venous as well as the arterial bed; consequently, the venous return as well as the arterial resistance is increased.

This patient had a second episode of shock for no apparent reason six days after the first episode. His response this time was again gratifying (Chart 3). It was possible to discontinue the *l*-arterenol after 21 hours of therapy. Again, transfusion alone did not correct the hypotensive state.

The outlook for this group of patients is generally considered poor when the condition remains untreated. In the two patients already cited, definitive surgery was performed and the patients recovered. It is not likely that these patients would

TABLE 2.—*Data on the Use of Arterenol in Twelve Patients with Surgical Shock*

Patient	Age, Yr.	Operative Procedure	Marked Blood Loss Present	Degree of Shock	Time of Onset of Shock	Av. Duration of Levophed Infusion, Hr.
J. C.	36	Pneumonectomy	Yes	Mild	Operative	7
E. D.	43	Repair of perforated sigmoid and colostomy	No	Moderate	Operative	1¼
R. K.	30	Lobectomy and thoracoplasty	No	Severe	Operative	4¼
E. V.	31	Lobectomy	Yes	Severe	Postop.	9
C. F.	50	Lobectomy and segmental resection	No	Mild	Operative	2
E. R.	20	Ileotransverse colostomy	No	Moderate	Postop.	8
P. J. R.	40	Ileostomy repair	No	Mild	Operative	1¼
A.	55	Cutaneous ureterostomy	No	Severe	Operative	12
A. R.	69	Prostatectomy	Probable	Severe	Postop.	68
McM.	73	Repair of perforated rectum	No	1. Moderate 2. Moderate	1. Operative 2. Postop.	49
S. K.	27	Abdom. perineal resection	No	Moderate	Operative	3¼
P. Q.	57	Ileotransverse colostomy	No	Severe	Postop.	8

have come to laparotomy without *l*-arterenol treatment, and they most certainly would have died.

Two patients died after surgery. One (W. H.) had uncontrolled peritonitis and mediastinitis from a perforation of the esophagus. The other (S. G.) was operated on for what was thought to be mesenteric thrombosis. This was not found, and autopsy failed to disclose any cause of the shock or death. In each case the treatment of shock was so satisfactory that necessary surgical procedures were attempted which could not otherwise have been done.

Of the two remaining patients, one (W. A. I.) with shock from generalized peritonitis recovered from his episode of shock but died four days later, probably from sepsis or fluid accumulation. The other (C. W. W.) had multiple small bowel perforation of unknown cause which followed closure of a perforation of the sigmoid. This condition was not amenable to current therapy and the patient died.

II. OPERATIVE AND POSTOPERATIVE SHOCK

In the 12 cases making up this particular group, moderate to severe shock developed in the course of or subsequent to extensive thoracic and abdominal operations. In three of the patients the state of shock was actually mild, but because of

the generally poor risk they represented and the extensive surgery to be carried out administration of *l*-arterenol was started early. Table 2 summarizes the most important data on the 12 cases of this group. A few illustrative case abstracts appear in the appendix.

Shock occurring during and after surgery may be due to hemorrhage, anesthesia, or the traumatic effect of the operative procedure. The role of hemorrhage will be discussed with the subsequent group of cases. Anesthesia causes shock most frequently through the predominant vasodepressor action of most anesthetic agents. Vasopressor substances such as phenylephrine have therefore gained considerable favor among anesthesiologists. We agree, however, with those[2] who consider *l*-arterenol superior to phenylephrine by virture of greater potency, easier controllability, and a more physiologic mechanism of its action.

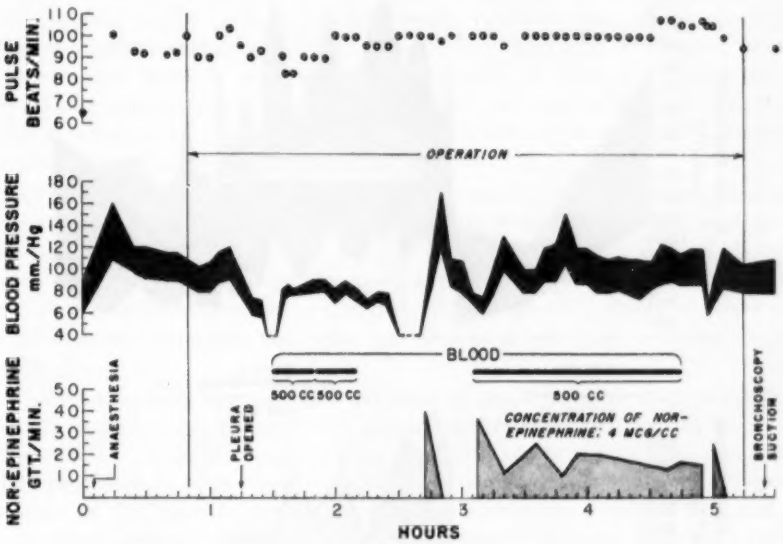

Chart 4.

Traumatic effects are particularly common in abdominal surgery, where they are usually due to traction on viscera,† and in intrathoracic surgery, where pleural pressure changes, mediastinal shift, or manipulation of the hilum may lead to shock.[5]

As regards the incidence of these factors in this second group of patients, anesthesia did not appear responsible for the shock encountered. Hemorrhage was a definite factor in two patients (V. C. and R. K.) and a probable one in another (P. J. R.). Adequate replacement of the blood loss did not abolish the state of shock in these patients, but the additional use of *l*-arterenol did.

Surgical trauma was probably responsible for the shock present in the remaining nine cases. Again, the pressor increment provided by the addition of *l*-arterenol to blood transfusion appeared very striking in the majority of the cases. Whenever

† References 5 and 6.

attempts were made to stop the *l*-arterenol infusion for the purpose of comparative observation, these patients would again show a drop of the blood pressure to shock levels. This occurred although a blood transfusion was in progress or was started promptly. Only the readministration of *l*-arterenol would raise the blood pressure to and keep it at normal levels (Chart 4).

III. HEMORRHAGIC SHOCK

The third group of patients present a variety of shock in which the use of a vasopressor is at present generally regarded as not only useless but even contraindicated. We have ourselves been very hesitant to use *l*-arterenol, but, confronted with a desperate situation, we proceeded with its use in one patient as a last resort.

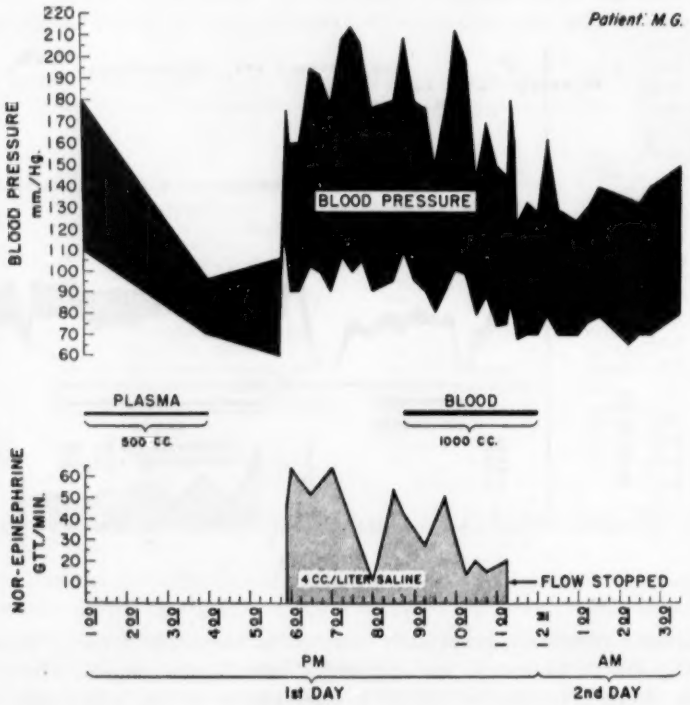

Chart 5.

M. G. (No. 1209) had a transurethral prostatectomy, after which, because of postoperative hemorrhage, transfusions were given. Two weeks later he started to bleed at the operative site. The bleeding continued for about 17 hours, during which time all attempts to cross match his blood with that of compatible donors failed. Because all available blood in the local area was incompatible, samples of his blood were sent to a central blood bank in New York City. During the time consumed by this procedure, the patient went into shock despite attempts to maintain him with infusions of plasma (Chart 5). At this time, with no blood available, the patient, whose normal tension was approximately 200/120, had a blood pressure of 105/60 and was stuporous and nonresponsive. His skin was cold and clammy, his eyes rolled up, and he appeared to be dying. When *l*-arterenol was administered, a very prompt rise in blood pressure occurred,

and with this change in blood pressure his clinical state appeared to improve markedly. He was maintained in good condition for two and one-half hours, at which time compatible blood arrived and he was given a transfusion. Five and one-half hours after *l*-arterenol was started, it was possible to discontinue the infusion, and the patient made a relatively uneventful recovery from this illness.

We observed two other cases of hemorrhagic shock with an equally striking response. In one patient (L. P., 19721) uncontrollable hemorrhage developed when adhesions about a carcinoma of the kidney were cut. The area was packed with oxidized cellulose, and further operation was abandoned. His severe shock was abolished successfully only after *l*-arterenol was added to the blood transfusions. The other patient bled profusely from a carcinoma of the stomach previously explored and found inoperable. He was brought out of shock and was enabled to undergo another prolonged operation with the aid of *l*-arterenol.

These cases taught us that patients in severe advanced hemorrhagic shock can exhibit a satisfactory pressor response to *l*-arterenol. This may be sufficient to tide them over until blood is available (Patient M. G.). It may also make possible surgical intervention which is indicated but cannot be undertaken unless the state of shock is removed (Patient P. S.). In all such cases treatment with *l*-arterenol constitutes part of a planned therapeutic program.

We wish to emphasize that *l*-arterenol must not be expected to abolish advanced hemorrhagic shock if the course of bleeding cannot be detected and eradicated. This was demonstrated to us most vividly in a young patient with massive bleeding from a peptic ulcer. The decision to operate was not made sufficiently early, and the patient died in spite of the administration of 13 pt. (6½ liters) of blood and the addition of *l*-arterenol. The latter was used as a last resort to make surgery possible.

The mechanism of the continued existence of shock in hemorrhagic patients is obscure. Actually most patients with hemorrhage respond satisfactorily to transfusion. There is, however, a small number of patients in whom peripheral circulatory failure progresses in spite of the replacement of the lost blood volume. It is beyond the scope of this paper to discuss the possible mechanisms involved. Suffice it to emphasize the general inapplicability of experimental work done on animals to the problem of shock in man, since it is extremely rare to find human beings subjected to the extreme measures employed in animals except during war or catastrophes.

GENERAL OBSERVATION AND COMMENT

Most of the standard texts dismiss the use of pressor agents in the treatment of shock or generally deprecate their use as unphysiologic. There is little validity to this contention, since studies of drug action on normal animals and humans cannot be transferred to shock patients. For example, a drug such as *l*-arterenol which in the normal human at normal intra-arterial pressures diminishes cerebral blood flow [7] cannot be said to do the same in a patient with markedly subnormal intra-arterial tension. Actually, the patient's improved mental status suggests that there is an improvement in the circulation. This improvement is a phenomenon observed with regularity. Similarly, although the total renal blood flow may be diminished in the normal human when given *l*-arterenol,[8] the constant increase in urine flow indicates that in the shocked human the increase in blood pressure resulted from *l*-arterenol

administration results in improved perfusion of the kidney. Similar reasoning applies to the coronary circulation ‡ where perfusion is so dependent on the aortic diastolic pressure.

When the clinical response of these patients as a group is viewed, several generalizations can be made. It can be readily observed that with the return of the blood pressure to normal the patient emerges from the symptom complex which characterizes clinical shock. The skin becomes drier and warmer, alertness returns, the pulse tends to slow, heart sounds become stronger, and the oliguria which is a constant concomitant of shock is replaced by an adequate urine flow.

The dramatic response of these patients is dependent upon the continuation of the infusion. Merely stopping it causes the reappearance of the hypotension and its satellite phenomena.

It is apparent, then, that the clinical manifestations of the shock state are directly dependent upon the level of intra-arterial tension. When this falls below normal, proper perfusion of tissues cannot occur, and the longer the resultant tissue anoxia lasts, the less likely is recovery. Thus it is our opinion that the use of *l*-arterenol to maintain a normal intra-arterial tension has an important place in the treatment of shock. It is worth while to note that not one of our patients has remained oliguric while undergoing treatment. This form of treatment, if properly applied, may possibly prevent the development of "lower nephron nephrosis."

The dangers of the use of *l*-arterenol are inherent in the potent effect upon the peripheral resistance regardless of the cause of the shock. One is likely to be lulled into a false sense of security by the promptness of the clinical response. Thus, it is essential that the cause of the shock state be known and definitive therapy undertaken as quickly as feasible. It is of special importance to rule out hemorrhage as the cause of shock. Lost blood must be replaced, and continued bleeding must be stopped. Otherwise the patient will exsanguinate while appearing to recover.

Another possibility of danger to be considered is the use of *l*-arterenol during cyclopropane anesthesia. Animal experiments have shown that *l*-arterenol may produce ventricular fibrillation during anesthesia with cyclopropane as readily as epinephrine. The clinical aspects of this problem are dealt with at length in a separate report.[9] Suffice it to state here that many of our patients have had cyclopropane anesthesia and without any untoward effect.

METHOD OF ADMINISTRATION

We have found that 8 ml. of a 1 : 1,000 solution of *l*-arterenol (that is, 8 mg. of *l*-arterenol in 1,000 ml. of isotonic sodium chloride or in 5% dextrose in distilled water) is safe and practicable. Blood or plasma may also be used. Where there is danger in administering large quantities of fluid, as in patients with diminished cardiac reserve or intracranial injuries, the concentration may be further increased to 16 and even 36 mg. of *l*-arterenol per 1,000 ml. of diluent. The blood pressure is observed carefully at 2 to 3 minute intervals until stabilization occurs, when readings are taken every 15 minutes. The rate of administration is easily checked by frequent counting of the drops per minute.

‡ Wegria, R.; Ward, H.; Frank, C. W., and Dreyfuss, F.: Unpublished data, cited by Goldenberg and co-workers.[2]

Two signs have proved of value in following patients being treated with *l*-arterenol. One is the pulse and the other, the blood pressure. The pulse returns to more normal values. This may not be observed, however, in atropinized patients. The second sign is the ability of the patient to maintain his own blood pressure when the infusion is stopped for about 10 or 15 minutes. If the systolic pressure remains above 90, it may be possible to stop the infusion.

Control of the administration is made easy by the fact that the blood pressure usually rises within a minute or so after the start of the *l*-arterenol infusion and drops within three minutes after the infusion is discontinued. The infusion with the drug may be kept up for many hours and even days. The only adverse reaction noted has been sloughing of skin, resulting from extensive soft tissue infiltration of the solution.[10] Hence, careful attention to the infusion site or infusion through a catheter extending into the superior vena cava is advisable.

SUMMARY AND CONCLUSIONS

l-Arterenol was given in continuous intravenous infusion to 22 patients in shock of different causes.

It was found of distinct value in cases of shock due to acute surgical abdominal conditions, in those with operative and postoperative shock, and in those with advanced hemorrhagic shock. It brough such patients out of shock when added to fluid replacement therapy which in itself had been ineffective.

The use of *l*-arterenol made it possible for some patients in profound shock to undergo extensive, and at times lifesaving, surgical procedures.

The method of administration is described. The response of the blood pressure and of the pulse rate are considered the best guides to the efficacy of this drug.

It is essential that the cause of shock be discovered prior to or early in the course of treatment lest a hidden hemorrhage should result in a fatal outcome.

APPENDIX

SHOCK ASSOCIATED WITH ACUTE SURGICAL ABDOMINAL CONDITIONS

W. A. I. (No. 1327), a 48-year-old white man, was considered to have an appendiceal abscess and was treated conservatively with antibiotics, etc. On the third day the patient suddenly went into shock and it was thought that the abscess had ruptured into the peritoneal space. He responded well to general supportive measures. On the sixth hospital day he suddenly went into shock again. Cortisone, 100 mg., was given I. M. Oxygen was administered in a tent and *l*-arterenol was started. On this regimen the blood pressure was maintained at normal levels. After 14 hr. *l*-arterenol could be discontinued. His general condition deteriorated, however, and he died of congestive heart failure on the 10th hospital day.

W. H. (No. 604), a 72-year-old white man, approximately 24 hr. after esophageal dilatation developed severe epigastric pain, a rigid abdomen, and rapidly advancing shock. A diagnosis of peritonitis was made, but operation was deferred because of the patient's profound shock and poor general condition. *l*-Arterenol infusion resulted in a prompt rise in blood pressure from 70/0 to 135/110; his condition improved, and exploration could then be done. He was found to have diffuse peritonitis, but the visceral perforation could not be found. He was maintained on *l*-arterenol therapy for 26 hr., when pulmonary edema developed and he died. Autopsy disclosed a fistulous tract extending from the esophagus to the peritoneum and the mediastinum and resulting in generalized peritonitis and mediastinitis.

S. G. (No. 1292), a 53-year-old white man with arteriosclerosis of the cerebral and coronary vessels, was hospitalized for chronic care. On Aug. 31, 1950, he suffered severe epigastric pain. Electrocardiogram at that time was interpreted as showing only an old posterior wall myocardial infarction. That evening he passed small amounts of bright red blood per rectum and went into mild shock, for which he was treated with 1 unit of plasma and 500 cc. of blood. His condition remained unchanged until five days later, when localized abdominal signs developed in the lower left quadrant, with generalized rebound tenderness. Surgery was considered impossible because of his poor condition. His blood pressure was 85/60; the following day, 70/30. *l*-Arterenol was started (8γ/cc.) at a rate of 25 to 35 drops a minute and continued until the next morning. During this time his blood pressure rose from 90/60 to 122/70; his pulse rate was 80, and exploratory laparotomy now became possible. When the abdomen was entered, about 200 cc. of bloody fluid was found. The small bowel was distended up to the ileocecal valve. There were several areas of purplish discoloration of the ilium thought to be due to many small mesenteric thromboses. The patient's abdomen was closed without any further surgery being done. During this time his blood pressure was maintained between 100 and 110 systolic and 50 diastolic; pulse rate 80 to 90, while between 30 and 50 drops (8γ/cc.) a minute of *l*-arterenol was administered. Patient did well until 6:30 a. m., when his pulse rate and blood pressure suddenly became unobtainable. There was no response to *l*-arterenol, and he died in 10 minutes. Postmortem examination did not reveal any cause for shock or death.

C. W. W. (No. 19877), a 50-year-old white man, was operated on for a large intestinal obstruction on Sept. 29, 1950, at which time a perforation of the sigmoid colon with fibrinous peritonitis were found. The opening was closed and a transverse colostomy done. He continued, however, to show evidence of obstruction. On Oct. 6, 1950, at 9:00 a. m. he appeared dehydrated, weak, lethargic; his blood pressure was 60/40, pulse rate 160. It was felt that the patient had a "chronic fatigue" state due to peritonitis, obstruction, and electrolyte imbalance. He received 2,000 ml. of isotonic sodium chloride solution and 500 ml. of blood without effect. He was then started on *l*-arterenol (4 mg. in 1,000 ml. of Ringer's solution, 120 drops a minute), and in five minutes his blood pressure rose to 110/70 and his pulse rate dropped to 120. An electrocardiogram was read as showing changes of hypopotassemia. This was corrected with Darrow's solution, as demonstrated by serial ECG's. Attempts to discontinue the arterenol infusion led to a drop of the blood pressure to 70/40. In spite of the gradually increased flow of arterenol over a period of 8 hr. shock set in again. The patient died in spite of further increase of arterenol. Autopsy revealed multiple small bowel perforations. This explains the ultimate irreversibility of shock.

OPERATIVE AND POSTOPETATIVE SHOCK

J. C. (No. 19276), a 36-year-old white man, had a left pneumonectomy on Sept. 15, 1950, for cystic disease of the lung. During the operation, the patient developed shock due to extensive bleeding. Although he received 7 pt. (3½ liters) of blood in continuous infusion, the blood pressure dropped from 120-140/65-100 to 80/60 and eventually to 60/40. *l*-Arterenol (4 mg. in 1,000 cc. isotonic sodium chloride solution) was started, with prompt response of the blood pressure. In spite of continued use of blood, the blood pressure could not be properly maintained without *l*-arterenol, which was given at a rate of 20 drops a minute. It was discontinued five and one-half hours after the operation.

Although in this instance shock may have been due mainly to the hemorrhage in the operative field, replacement of the lost blood did not appear adequate by itself to abolish the shock state. *l*-Arterenol seemed to possess a definite preventive and therapeutic effect.

R. K. (No. 12897), a 30-year-old Negro, was subjected on May 12, 1950, to left upper lobectomy and thoracoplasty with removal of the first four ribs for cavitary tuberculosis (Chart 4). About 1 hour 40 minutes after the operation started, the blood pressure became unobtainable as the pleura was opened. The administration of 1,000 cc. of blood was able to raise it to 80/40 for only very short periods. Administration of *l*-arterenol led to a prompt rise of the blood pressure to, and maintenance at, about 120/90. It was given in continuous infusion throughout the rest of the operation and for 1 hour afterward. During this period he also received an additional 1,500 cc. of blood. The total blood loss incidental to the operative procedure was estimated at 2,000 cc.

E. R. (No. 19936), a 20-year-old white man, underwent laparotomy on Dec. 18, 1950, because of ileocecal ulceration with formation of fistulas. An ileotransverse colostomy with

resection of the ilium was done. He went into shock postoperatively; the skin was cold and clammy, the pulse rate 120, and the blood pressure 82/60. He had received 1,000 cc. of blood and 1,300 cc. of 5% dextrose in water during the operation. An additional 500 cc. of blood failed to change his condition. *l*-Arterenol was then administered (8 mg. in 1,000 cc.), with prompt rise of the blood pressure. When it was discontinued for a period of 10 minutes and another 500 cc. of blood started, the blood pressure fell again to shock levels. When discontinued again about eight hours later, the blood pressure dropped to shock levels (74/38) in spite of the administration of another 500 cc. of blood. *l*-Arterenol was therefore restarted and maintained for two hours, when spontaneous control was established.

E. V. (No. 18299) a 31-year-old Negro, was subjected to decortication and segmental resection of the left upper lobe on Oct. 27, 1950. About 45 minutes after the uneventful operation the patient went into shock. His B. P. was unobtainable. An infusion of *l*-arterenol (8γ/cc.) was started. Within a few minutes his blood pressure rose to 110/78. This infusion was alternated with 2,000 cc. of whole blood for nine hours. Blood transfusion alone could not maintain the blood pressure. It fell to 78/20, the pulse rate rose to 140, and the patient lapsed into semiconsciousness. Later the patient seemed able to maintain a normal blood pressure while 1,000 cc. of blood was administered during the following three hours. His B. P. dropped again precipitously to 76/56, and the pulse rate rose to 120, when patient was positioned for a chest film. *l*-Arterenol promptly returned his B. P. to normal. It was continued for 25 minutes with the B. P. staying at 112-120/78-90. His further postoperative course was uneventful.

The shock proved to be related to a massive left hemothorax of which about 1,000 cc. drained through the chest catheters. The patient had received a total of 3,000 of blood and 200 cc. of 5% dextrose in distilled water in the first 16 hours postoperatively. However, only the addition of a total of 400 cc. of *l*-arterenol appeared to abolish the shock state.

McM. (No. 7287), a 73-year-old white man, had an exploratory laparotomy on Jan. 4, 1951, and a perforation of the rectum was found with fecal soiling of the peritoneum. Shortly after the onset of the operation his B.P. fell to 85/60. Blood, 500 cc., administered rapidly brought the B.P. to 96/65, but it soon fell again to 80/60. *l*-Arterenol was started and the B. P. rose to 140/80. An additional 500 cc. of blood was given. *l*-Arterenol was stopped at the end of the operation. During the night the patient's condition deteriorated slowly despite the administration of 500 cc. of blood and 2,000 cc. of 5% dextrose in distilled water. The B. P. fluctuated between 80-100/60 and the pulse rate between 90 and 120. The urinary output was 175 cc. for the first 16 postoperative hours. The oliguria was thought to be due to hypotension or a hemolytic reaction. *l*-Arterenol (4γ/cc.) was then given for 49 hours. The B. P. stabilized at about 120/70 and the urinary output rose to 345 cc. in the first eight hours and 300 and 480 cc. in subsequent eight-hour periods.

A. R. (No. 4541), a 69-year-old white man, was subjected to a transurethral prostatectomy on Aug. 7, 1950, and four and one-half hours postoperatively he became restless; his B. P. fell to 70/40 and the pulse rate rose to 144. He was put in Trendelenburg position and given 500 cc. of blood and 600 cc. of dextrose in distilled water. He remained in shock during that night, and the following morning (14 hours after onset of shock) his B. P. was 60/40, pulse rate 124, and urinary output nil. He had been given adequate doses of antibiotics and nikethamide and was in an oxygen tent.

Electrocardiogram taken at this time showed T wave inversions in V 3-6. The chest film showed hilar and basal congestion. Physical examination disclosed a patch of rales at the right lung base and an area of tenderness in the left calf with a positive Homan's sign. The temperature was 100 F., pulse rate 125, WBC 32,600.

The cause of the shock was not clear. Because of the possibility of pulmonary embolism, heparin and bishydroxycoumarin were given. *l*-Arterenol was started (8 mg. in 1,000 cc. 5% dextrose in distilled water). The B. P. rose promptly from 70/50 to 104/64. The arterenol infusion was continued throughout the morning and by 3:00 p. m. he had voided 600 cc. of urine. After this, 1,000 cc. of blood and 1,000 cc. of dextrose in saline was given.

The following day the patient was definitely improved. The electrocardiogram showed return of the T waves to normal. Fluid and electrolyte balance were maintained, and 68 hours after the beginning of *l*-arterenol he regained spontaneous vasomotor control, and the medication was discontinued.

The significant observations in this case were (1) the return of the urine flow following the elevation of the blood pressure, (2) the reversal of T wave changes in the electrocardiograms within 24 hours after the blood pressure was made normal, and (3) the prolonged period of treatment necessary (68 hours).

REFERENCES

1. Goldenberg, M.; Pines, K. L.; Baldwin, E. deF.; Greene, D. G., and Rah, C. E.: The Hemodynamic Response of Man to Nor-Epinephrine and Epinephrine and Its Relation to the Problem of Hypertension, Am. J. Med. **5**:792, 1948.

2. Goldenberg, M.; Apgar, V.; Deterling, R. A., Jr., and Pines, K. L.: Nor-Epinephrine (Arterenol, Sympathin N) as a Pressor Drug, J. A. M. A. **140**:776, 1949.

3. Luger, N. M.; Kleiman, A., and Fremont, R. E.: Treatment of Shock with Arterenol, J. A. M. A. **146**:1592, 1951.

4. Fremont, R. E., and Stellar, S.: The Use of Arterenol in the Treatment of Shock in Neurosurgical Patients, to be published.

5. Davis, H. A.: Shock and Allied Forms of Failure of the Circulation, New York, Grune & Stratton, Inc., 1949.

6. Richards, D. W., Jr.: Circulation in Traumatic Shock in Man, Harvey Lect. **39**:217, 1944.

7. Sensenbach, W.; Madison, L., and Ochs, L.: Effect of Arterenol on the Cerebral Circulation in Normotensive Males, abstracted, Am. J. Med. **11**:250, 1951.

8. Barnett, A. J.; Blacket, R. B.; Depoorter, A. E.; Sanderson, P. M., and Wilson, G. M.: The Action of Noradrenaline in Man and Its Relation to Pheochromocytoma and Hypertension, Clin. Sc. **9**:151, 1950.

9. Surks, S. N., and Luger, N. M.: Clinical Use of *L*-Arterenol During Cyclopropane Anesthesia, to be published.

10. Greenwald, H. F.: Gootnick, A.; Luger, N. M., and Kings, J. A.: Tissue Necrosis Following Subcutaneous Infiltration with Arterenol: Report of Two Cases, New England J. Med. **246**:252, 1952.

EXPERIMENTAL REPAIR OF URETERS BY POLYETHYLENE TUBING AND URETERAL AND VESSEL GRAFTS

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OCCASIONALLY the surgeon is confronted with the vexing problem of restoring a gap in the ureter. If the defect is extensive, he must be content with a choice of either nephrectomy, cutaneous ureterostomy, uterosigmoidostomy, or ureteroureteral anastomosis.[1] A defect of the distal ureter near the bladder can be reconstructed by utilizing a full-thickness flap of bladder wall fashioned into a tube.[2]

Experimentally, segments of the ureter have been successfully bridged by the substitution of a loop of terminal ileum.[3] The transplantation of dog ureters into the duodenum caused death from electrolyte imbalance.[4] Vitallium [5] and fascial transplants [6] have been used as a direct method of reconstructing ureteral defects. Vitallium tubes are reported to be tolerated in the urinary tract of the dog for as long as nine months without causing encrustrations. End-to-end anastomosis of the ureter over a straight Vitallium tube healed per primam in each instance. Free fascial grafts over a straight Vitallium tube with an attached holder were used to span ureteral defects. The flanged holder was necessary to prevent the migration of the tube. Whenever the tube migrated, a stricture formed in the fascial graft. Free peritoneal and bladder grafts failed in every experiment because of sloughing.

The following experiments were undertaken in an attempt to expand the methods by which ureteral defects could be repaired.

GENERAL OPERATIVE PROCEDURE

Twenty-five mongrel dogs were operated on with the use of intravenous pentobarbital (Nembutal) sodium anesthesia. A left flank incision was used to expose the ureter transperitoneally in those experiments in which polyethylene substitution was done. These wounds were closed without drainage. A retroperitoneal approach to the lower one-third of the ureter was utilized in bridging surgical defects with homologous ureteral or vessel grafts. The operative field was drained except in those dogs having an internal splint catheter for drainage. Penicillin procaine, 300,000 units daily, was given for one week after surgery. Contralateral nephrectomies were done from 5 to 14 days after ureteral substitution as a control method.

COMPLETE SUBSTITUTION OF THE URETER BY MEANS OF POLYETHYLENE TUBING

Polyethylene tubing seemed to possess the ideal physical and chemical properties for a permanent ureteral prosthesis [7] (Table 1). This plastic material has excellent tissue tolerance in its pure state, and is nonwetting.* Since polyethylene is inert, urinary encrustations should not form in the lumen of the tube. Polyethylene catheters used for constant urethral and ureteral drainage have received favorable clinical reports.[10]

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* References 8 and 9.

Method

In six dogs the ureter was excised at the renal pelvis and bladder wall. The defect was bridged by means of polythylene tubing ranging in length from 15 to 19 cm. The internal diameter of these tubes varied from 0.86 to 1.67 mm. The ends of the polyethylene tubes were flanged by passing each end through an alcohol flame. A purse-string suture was placed in the wall of the renal pelvis and bladder to encompass the site of ureteral excision. The flanged ends of the tubing were then inserted; the purse-string sutures were tied, and the flanged ends of the tubes were withdrawn to engage the internal wall of the bladder and renal pelvis.

Table 1.—*Complete Substitution of the Ureter by Means of Polyethylene Tubing*

Dog No.	Length of Tubing, Cm.	Internal Diameter of Tubing, Mm.	Contralateral Nephrectomy After Substitution, Days	Fate of Animal	Postmortem Findings
44	15	1.40	12	Killed 21 days	Moderate hydronephrosis, lumen patent
69	18	1.14	12	Died 34 days	Proximal stenosis pelvic site; distal migration of tubing, marked hydronephrosis
30	15	0.86	5	Killed 43 days	Moderate hydronephrosis, lumen patent
59	19	1.19	13	Died 43 days	Proximal stenosis pelvic site; complete obstruction; pelvis filled with pus; marked hydronephrosis
31	15	1.57	10	Died 50 days	Complete distal obstruction by bladder
29	18	1.67	10	Died 45 days	Same as above wall; marked hydronephrosis

Table 2.—*Urinary Diversion to the Sigmoid by Means of Polyethylene Tubing*

Dog No.	Length of Tubing, Cm.	Internal Diameter of Tubing, Mm.	Contralateral Nephrectomy After Substitution, Days	Fate of Animal	Postmortem Findings
68	12	0.86	14	Died 17 days	Distal end extruded from sigmoid wall; proximal end closed with scar tissue; severe hydronephrosis
64	14	1.77	10	Died 34 days	Distal end occluded by scar tissue; marked hydronephrosis
28	15	1.14	11	Died 56 days	Leakage around distal insertion to sigmoid; free urine and feces in abdomen; marked hydronephrosis
61*	15	2.69	8	Killed 65 days	Marked hydronephrosis, lumen patent
60*	14	2.92	10	Died 75 days	Marked hydronephrosis, lumen patent

* Polyethylene tubing substituted for ureter from pelvis to sigmoid.

Results

Two dogs were killed at 21 and 43 days. The lumen of the tubes were free of encrustations, but moderate hydronephrosis was present. The four remaining dogs died from 34 to 50 days, owing to the effects of complete cicatricial obstruction of the polyethylene tubes. The tubing migrated either proximally or distally, closing the lumen with scar tissue. Severe hydronephrosis was noted in each of these four dogs.

URINARY DIVERSION TO THE SIGMOID BY MEANS OF POLYETHYLENE TUBING

In three dogs the distal ureter was ligated at its vesicoureteral junction (Table 2). The proximal ureter was excised 2.5 cm. from the renal pelvis. A flanged polyethylene tube was inserted into the ureteral segment and was secured with two 0000 nonabsorbable surgical (black

silk) ligatures. A purse-string suture of 0000 black silk was made in the wall of the sigmoid, and a stab incision was made into the bowel. The distal end of the flanged tube was inserted into the lumen of the bowel. The purse-string suture was tied to create a watertight seal. Additional interrupted sutures of 0000 black silk were added for a distance of 1 cm. to cover the extraluminal portion of the tube with bowel serosa. Two dogs had urinary diversion from the renal pelvis to the lumen of the sigmoid. The artificial plastic ureters varied in length from 12 to 15 cm. The internal diameters ranged from 0.86 to 2.92 mm.

Results

All five of the dogs died or were killed over a period ranging from 17 to 75 days. In two dogs the distal end of the polyethylene tube was extruded from the wall of the sigmoid. The lumens of the tubes were occluded by scar tissue. In one dog pressure necrosis caused urinary and fecal drainage around the plastic tube. In the two remaining animals the lumen of the tube was free of encrustations. All of the animals showed marked hydronephrosis at the time they were killed or died.

HOMOLOGOUS URETERAL GRAFTS

Five dogs had defects in the ureter, 3 to 5 cm. in length replaced by fresh homologous grafts (Table 3). Interrupted 000000 black silk arterial suture was

Table 3.—*Homologus Ureteral Grafts*

Dog No.	Length of Graft, Cm.	Catheter Splint Drainage	Contralateral Nephrectomy After Graft, Days	Fate of Animal	Postmortem Findings
24	3	7 days	10	Killed 21 days	Beginning stenosis
19	4	None	7	Died 30 days	Free urine in abdomen, dehiscence distal suture line
23	4	7 days	12	Killed 55 days	Complete stenosis of graft; moderate hydroureter and hydronephrosis
20	3.5	None	7	Died 65 days	Complete stenosis; severe hydroureter and hydronephrosis
18	5	None	10	Died 70 days	Complete stenosis; severe hydroureter and hydronephrosis

used for the anastomosis. Two dogs had internal polyethylene catheter drainage for seven days. Distally the catheter extended beyond the graft for 2 cm. The splint catheter was passed proximally through the ureter and renal pelvis and then was brought out the left flank through a separate incision. Two lateral drainage sites were made in the wall of the polyethylene catheter which passed through the renal pelvis.

Results

This group of animals died or were killed from 21 to 70 days. Four of the homologous grafts failed because of stenosis. One graft showed dehiscence at the suture line owing to nonviability. All of the homologous grafts were thickened by marked external fibroplasia. Severe hydronephrosis was seen in those animals with complete stenosis of the graft.

AUTOGENOUS FEMORAL ARTERY AND VEIN GRAFTS TO URETERAL DEFECTS

Ureteral defects ranging from 2.5 to 5 cm. were replaced with autogenous femoral artery or vein grafts in 10 dogs (Table 4). Six of the grafts had internal

polyethylene splint drainage. The free vein grafts were rotated 180 degrees in order to eliminate any obstruction from a valve.

Results

This series of dogs died or were killed from 21 to 58 days. The contributing causes of death were stenosis, degeneration of the graft, and leakage at the suture lines. Proximal hydroureter and hydronephrosis were severe whenever stenosis was present. The free femoral vein grafts showed much more adventitial fibroblastic proliferation than the free artery grafts.

Comment

The experimental use of polyethylene tubing as a permanent ureteral prosthesis proved unsuccessful. The plastic tubing, however, did remain free of encrustations. Migration of the rigid plastic tubes from the renal pelvis, bladder, or bowel led to blockage of the lumen by scar tissue. In those animals in which the plastic tubes did not migrate the effects of hydronephrosis were evident. In order to eliminate this complication polyethylene tubes with a larger internal lumen were used to

Table 4.—*Autogenous Femoral Artery and Vein Grafts to Ureteral Defects*

Dog No.	Length of Graft, Cm.	Catheter Splint Drainage	Contralateral Nephrectomy After Graft, Days	Fate of Animal	Postmortem Findings
65	3	10 days	10	Died 21 days	Free urine in abdomen; dehiscence of proximal suture line
64	3	None	11	Died 30 days	Complete stenosis; marked hydroureter and hydronephrosis
52	3	None	7	Died 25 days	Free urine in abdomen; dehiscence of distal suture line
63	2.5	None	12	Died 35 days	Free urine in abdomen; complete degeneration of graft
131	3.5	21 days	12	Killed 45 days	Beginning stenosis of graft, mild hydroureter and hydronephrosis
66	2.5	14 days	12	Died 54 days	Complete stenosis; marked hydroureter and hydronephrosis
67	3.5	7 days	10	Died 58 days	Same as above
50*	5	7 days	7	Died 21 days	Distal leakage into abdomen
47*	4	7 days	10	Killed 30 days	Beginning stenosis
49*	3	None	12	Died 45 days	Complete stenosis, hydroureter and hydronephrosis complete
57*	3.5	None	12	Died 50 days	Same as above

* Dogs receiving autogenous vein grafts to ureteral defects.

provide a more efficient dependent urinary drainage. This also failed, thus reemphasizing the fact that hydrodynamics alone cannot account for the passage of urine from the renal pelvis to the bladder.

Normally the urine is collected in the true renal pelvis and is ejected into the ureter by pelvic compression of the detrusor muscle. The urine then passes down the ureter in a staggered peristaltic wave.† The complete substitution of the ureter by a rigid plastic tube completely eliminates the physiologic peristalsis of the ureter and causes varying degrees of hydronephrosis.

Homologous ureteral grafts failed because of stenosis, dehiscence, or leakage. Such a free transplant is dependent on contiguous tissue for its vascularization.

† References 11 and 12.

By the time proliferating capillary vascular buds have permeated the free graft, necrosis and scar formation already have taken place. The hydrostatic pressure of the ureteral urinary flow is not sufficient to overcome the contractile process. One must also consider the antigenic dissimilarity of the homologous ureteral grafts as a contributing cause for failure.

Autogenous vessel grafts were selected for bridging ureteral defects in order to overcome antigenic tissue incompatibility. This series of free grafts again failed primarily because of a lack of vascularity. Our previous attempts at bridging common bile duct defects in the dog with free grafts also failed for the same reason.[13] The suggested experimental substitution of a terminal ileal loop[3] with its intrinsic blood supply would seem to have promise in bridging extensive ureteral defects.

SUMMARY

The experimental substitution of polyethylene tubing, homologous ureteral grafts, and autogenous vessel grafts for bridging ureteral defects proved unsuccessful. The plastic prostheses migrated or abolished normal ureteral peristalsis producing hydronephrosis. Free grafts failed because of an adequate blood supply or tissue incompatibility.

REFERENCES

1. Higgins, C. C.: Transuretero-Ureteral Anastomosis, Tr. Am. A. Genito-Urin. Surgeons **27**:279, 1934.

2. Ockerblad, N. F.: Reimplantation of the Ureter into Bladder by Flap Method, J. Urol. **57**:845, 1947.

3. Davids, A. M., and Lesnick, G. J.: Experimental Reconstruction of Ureters by Substitution of Small Bowel Segments, Ann. Surg. **137**:389, 1953.

4. Hinman, F., and Belt, A. E.: An Experimental Study of Uretero-Duodenostomy, J. A. M. A. **79**:1917, 1922.

5. Lord, J. W., Jr., and Eckel, J. H.: The Use of Vitallium Tubes in the Urinary Tract of the Dog, J. Urol. **48**:412, 1942.

6. Lord, J. W., Jr., Stefko, P. L., and Stevens, A. R.: On Bridging a Gap in the Ureter by Means of a Free Fascial Transplant over a Straight Vitallium Tube. An Experimental Study, J. Urol. **49**:249, 1943.

7. Ingraham, F. D.; Alexander, E., and Matson, D. D.: Polyethylene, a New Synthetic Plastic for Use in Surgery, J. A. M. A. **135**:82, 1947.

8. Hufnagel, C. A.: Permanent Intubation of the Thoracic Aorta, Arch. Surg. **54**:382, 1947.

9. Matson, D. D.: A New Operation for the Treatment of Communicating Hydrocephalus: Report of a Case Secondary to Generalized Meningitis, J. Neurosurg. **6**:238, 1948.

10. Ferris, D. D., and Grindlay, J. H.: Use of Polyethylene and Polyvinyl Tubing in Ureterostomy, Nephrostomy, and Cystostomy, Proc. Staff Meet., Mayo Clinic. **23**:385, 1948.

11. Narath, P. A.: Renal Pelvis and Ureter, New York, Grune & Stratton, Inc., 1951.

12. Muschat, M.. Musculus Spiralis Papillae: The Milking Muscle of the Renal Papilla, J. Urol. **16**:351, 1926.

13. Hardin, C. A., and Kittle, C. F.: The Experimental Use of Free Arterial and Split Thickness Skin Grafts for Bridging Defects in the Common Bile Duct of the Dog, Surg. **30**:834, 1951.

PRESENT STATUS OF CARCINOMA OF THE PANCREAS

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THE MONUMENTAL work of Whipple in which he devised the surgical technique of the pancreatoduodenal resection for carcinoma of the pancreas has stimulated surgical interest in a heretofore ominous tumor site. Since the report of his work in 1935,[1] a number of surgeons throughout the country have been carrying out this procedure. Very few surgeons, however, have had extensive experience in the radical resection of this carcinoma because, while the tumor is not uncommon, only rarely do we find a suitable candidate for radical surgery.

Analyses of our results obtained in the Swedish Hospital and of those reported in the literature * are difficult to evaluate accurately. In the first instance, we are dealing with an organ whose function is vital to a normal digestive physiology. In the second place, the anatomical location of the pancreas, with its duct system exhibiting a high incidence of developmental anomalies and with variations in the exact anatomical site of the tumor, the age of the patient, and the dependent relationship of the pancreas with the duodenum and biliary tract, together with extreme disparity in individual fat nutritions, make statistical appraisal difficult.

Most important and too frequently overlooked is the third point, and that is the biological behavior of the tumor. In spite of very careful dissection and apparent complete removal of the local tumor a large percentage of patients die rapidly of widespread metastases. I have been disappointed with my results, and I am certain many will share this disappointment with me. The following is an evaluation of the results of surgical therapy in proved cases of this disease at the Swedish Hospital from 1947 through 1952.

The chief problem is to reduce morbidity by surgery in carcinoma of the pancreas and to palliate rather than mutilate. We must not, however, overlook an opportunity for obtaining maximum results in favorable cases by a radical removal of these carcinomas. With surgery as our only therapeutic tool we are faced with utilizing the radical or conservative approach in our so-called plan of attack.

It is obvious at this point that any analysis must include a careful appraisal and selection of every case on the basis of the patient's general condition and the anatomical site and local behavior of the tumor. These points should determine, in my opinion, a radical versus a conservative approach to carcinoma of the pancreas, duodenum, ampullary, or biliary carcinoma.

Anatomical variations will be found frequently. For example, the carcinoma in the head of the pancreas will probably be diagnosed earlier because of pertinent diagnostic signs than one in the tail of the pancreas, but given a resectable lesion

* References 2, 3, and 4.

in each position the latter is more favorable. The carcinoma of the pancreatic head is usually more advanced when seen at operation than the carcinoma of the ampulla of Vater or lower common duct carcinomas. Because of their location, they will produce early obstruction of the common duct, resulting in the acute onset of jaundice and in earlier detection of the lesion. The ultimate results with these lesions are also much more favorable than with lesions in the head of the pancreas. However, in our series, 93% of the tumors occurred in the region of the head of the pancreas.

Often the surgeon attempting to evaluate the location and extent of the disease finds himself doing a radical procedure when he simply had an investigation of the tumor in mind at the onset. We have all had the unfortunate experience of undertaking a resection in good faith and during the procedure becoming aware of areas of extension involving vital structures not apparent when the decision for extensive surgery was made. It is not remarkable, then, that a review of the available statistical evidence reveals that about 75% of these patients have a lesion that cannot be removed radically, and I find in my own experience that 83% fall into this category. One must judge resectability absolutely on an individual anatomical basis, depending on extent, location, etc., which can in no instance be done prior to exploration.

The factors of judgment in determining the fitness of the patient for surgery must obviously be considered here as in any major surgical procedure. The jaundiced patient always presents the problem of diagnosis, but, aside from this, in evaluating him as a surgical prospect, we must pay very strict attention to the status of his liver. Does he have evident liver damage, and, if so, exactly what surgical procedure will be tolerated? You will find present-day liver function studies not only valuable in the assessment of the patient's ability to endure surgery but, also indispensable as diagnostic guides. Can we expect to receive accurate and valuable diagnostic help from the roentgenologist? Our x-ray department believes their contributions will be very minimal because the diagnosis of carcinoma of the pancreas will be obvious clinically by the time they can demonstrate without question a so-called reverse three sign. A space-occupying lesion in this area is not necessarily diagnostic of a carcinoma of the pancreas.

Too often we have a set pattern of operative behavior mapped out before surgery and make our case fit the operation rather than inspecting our problem and selecting a proper procedure. Obvious extension necessitates selection of a proper palliative procedure where necessary. Any involvement beyond the strict confines of the pancreas or immediate adjacent duodenum, as in adjacent organs such as the portal vein, superior mesenteric vessels, or paravertebral structures, means inoperability, as far as I am concerned. This is contrary to some excellent surgical thought on this problem. Some inspection may be necessary to demonstrate this spread, but if it is demonstrable it is best to resort to a palliative operation. Opening of the duodenum may be necessary for proper inspection in certain instances and may avert an error that our surgical department made. A gallstone had become impacted at the ampulla; chronic pancreatitis resulted, and the surgeon did a pancreatoduodenectomy for what he considered a carcinoma of the head of the pancreas.

Are we to expect any success in palliation with the radical approach to this problem? McDermott,[5] from the Massachusetts General Hospital, reported on 33 patients with pancreatoduodenectomy who had an average survival time of 11

months, as compared with 70 patients with conservative palliative shunt operations whose average survival time was 4 months. It is pointed out that the patients subjected to resection are perhaps a group in whom the disease either is in an earlier stage of development or whose tumors have a slower manner of growth and therefore are not comparable to a group in whom only palliative surgery was considered feasible.

Has the radical pancreatoduodenal resection altered the natural history of carcinoma of the pancreas? We have good evidence from all reported series that it has not. The five-year survivors of the radical operation are for practical purposes nonexistent. The problem lies in the behavior of this tumor rather than in the extent of operation, as is emphasized by a recent case in the surgical service of the Swedish Hospital. The surgeon after doing a pancreatoduodenectomy was told by our pathologist that grossly the specimen had the appearance of chronic pancreatitis. It was only on microscopic study that the true nature of the lesion was revealed, and then in only 1 of 40 serial sections made was there evidence of carcinoma of the pancreatic ducts. This patient, in spite of a minimal carcinoma, was dead in six months of metastatic disease, which emphasizes the virulence of this pancreatic tumor and the complete failure of extremely early radical surgical therapy in this instance. The outlook for carcinomas of the lower common duct, ampulla of Vater, and duodenum is much more favorable. In the absence of local infiltration or distant metastases every effort should be made to extirpate them.

Differentiating pancreatitis from carcinoma is often a very real enigma, as they both may occur in the same patient. I have already discussed two problem cases. What then should our attitude be regarding biopsy with frozen section as a guide at the operating table? The greatest objection is the fact it is often misleading and false impressions are obtained. Frozen sections of the pancreas are difficult to interpret and are inaccurate. A small early carcinoma, deeply placed and surgically favorable, may be missed by a superficial biopsy of the overlying inflammatory pancreas. There is the additional danger of continued pancreatic leakage. Mathewson,[6] reporting the Stanford Hospital series, recorded an example of this type of error that I believe bears reporting here. The patient had on his first operation a biopsy taken with reported frozen section diagnosis of chronic pancreatitis. A cholecysjejunostomy was performed for biliary drainage. Permanent sections two days later were reported as carcinoma of the pancreas; consequently, a radical resection was then undertaken. The resected specimen revealed no tumor. At necropsy, eight months later, the original tumor proved to be metastatic adenocarcinoma in a retroperitoneal lymph node from a carcinoma of the sigmoid colon.

The problem of selection of suitable candidates for the mechanical performance of pancreatoduodenectomy could easily be solved if we were able to predict the ones in which the condition will become complicated and reserve operation for the remainder. The two most distressing complications are the fistula and the abscess secondary to a leaking anastomosis. It has been aptly stated by Baker † that these complications usually are the result of technical imperfection and can almost be prophesied by the comfortableness of the exposure at the onset. Such exposure depends on a number of things, such as obesity and depth of field, fat infiltration of the mesenteries, body build, etc. A one-stage procedure in the good-risk patient

† Baker, J. E., in discussion on Mathewson.[6]

has definite and obvious advantages over the two-stage. However, a biliary short-circuiting operation is invaluable as a first stage in the patient with obstruction and long-standing jaundice. It does two things. First, it allows the patient's liver an opportunity to recover from long-standing damage and thereby increases the number of surgical survivals. Second, it permits the surgeon who does not care to do a radical resection the opportunity to perform a first-stage operation at the initial exploration when he is confronted with a biliary obstruction from a carcinoma of the pancreas. Therefore it places a definite responsibility upon him for doing a biliary shunt when this situation is encountered.

It is impossible always to differentiate at surgery the favorable lower bile duct, ampullary, or duodenal carcinomas from the unfavorable carcinomas of the pancreas. Therefore in patients whose lesions have not spread beyond the confines of the gland or the adjacent portion of the duodenum and in whom the procedure can reasonably be carried out from a technical standpoint, we are obligated to do a pancreatoduodenectomy. For those not fitting into this category palliation by a shunt procedure is done, and in those with impending duodenal obstruction, a gastroenterostomy.

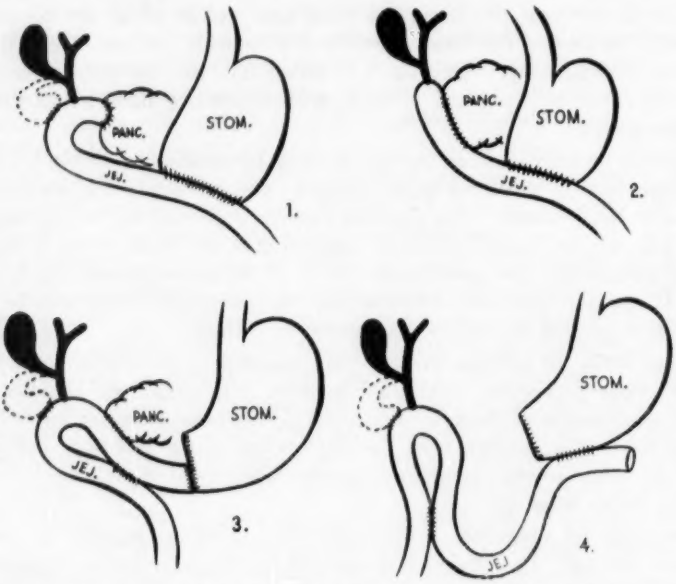
From the technical lessons learned in doing pancreatoduodenectomies, there are a few basic facts of which we must be aware. The pancreatic duct should be anastomosed to the jejunum. This pancreatic anastomosis and the biliary anastomosis to the jejunum, be it gall bladder or common duct, are better in most instances if they are proximal to the gastrojejunostomy. If the gastrojejunostomy is proximal to the biliary and pancreatic anastomosis, an enteroenterostomy will be valuable in partially isolating the biliary and pancreatic orifices.

In our series 10 patients, or 62%, had one-stage pancreatoduodenal resection. The two-stage procedures were used in those with prolonged jaundice or with marked enlargement of the liver and in one elderly patient considered to be a poor surgical risk. It is apparent that the employment of the two-stage operation has enabled us to extend the operation to patients who would not otherwise be suitable risks for major surgery.

How radical a procedure is one justified in doing, as regards the amount of pancreas resected? In a lesion well selected for surgery that is localized to the pancreatic head, we believe that partial pancreatoduodenectomy does not have the subsequent disabling effects of total pancreatectomy. Cole [7] explains early recurrence with favorable lesions on the basis of free malignant cells in the obstructed duct of Wirsung. Thus dissemination of carcinoma occurs by cutting across the duct, with the escape of pancreatic fluid, which could be averted with total pancreatectomy. In only three of our cases was total pancreatectomy done. In the remaining cases there was no evidence of tumor at the transected end either in the pancreatic duct or in the glandular tissue, thus making us feel that we have been employing sufficiently radical surgery and yet are being reasonably considerate of the future physiological processes in a person with a carcinoma of fatal biological potential.

The surgical staff of the Swedish Hospital, with the encouragement of the pathological department, has since 1947 adopted a very rigid attitude toward radical resection and has used it only in the most favorable cases. Local invasion of surrounding structures or demonstrable metastases in distant organs or regional

lymph nodes has contraindicated radical surgery. In spite of this, our survival figures are no better than parallel to those in comparable series in which the indications were more liberal.[8] We have one four-year survivor, a patient in whom there is pathological disagreement as to whether the tumor should be classified as originating in the ampulla or in the pancreatic head proper. We do know, however, that a minimal number of patients received unrewarding surgery and that a maximum number received all that surgery had to offer them. The resectability rate for carcinoma of the pancreas, in our hands, was 23%. Our over-all operative mortality with pancreatoduodenal resection for carcinoma of the pancreas was 26%. In the patients with resection for ampullary carcinomas or in those with benign lesions on whom resection was inadvertently done there were no operative deaths.



Techniques most frequently used in pancreatoduodenal resection in this series.

The conservative approach to the treatment of carcinoma of the pancreas arises from the desire of some surgeons to make a bad situation no worse. It consists in the shunting of bile around the obstructing tumor when necessary and returns the patient to his family for a temporary period, relatively happy. Advocates of this method are encouraged by the poor survival record in those successfully treated by the radical procedure, and they point with reason to the appreciable mortality rate of this procedure in ordinary hands. The morbidity rate from digestive disturbances, cholangitis, leakage, and fistulae, plus the overwhelming financial burden of long hospitalization, is considerable. Furthermore, with this method no benign lesions will be mistaken for carcinoma and erroneously resected. It is obvious that such conservative management overlooks the relatively favorable ampullary, duodenal, and lower bile duct carcinomas and removes this small group from any possibility of long-term survival.

The technique of the palliative procedure will be determined in each instance by the local findings. Any palliative procedure should be simple and involve a minimal number of anastomoses, since the patients have extensive tumors and are poor risks (Figure). If we keep the procedures simple, we will not hesitate to employ them. Cholecystjejunostomy, utilizing a comfortable length of jejunum, is the procedure of choice. In our series it was used twice as frequently as all the other shunting operations. If the gall bladder is absent or is unsuitable to anastomose, then choledochostomy is satisfactory although technically somewhat more difficult. Actual or impending duodenal obstruction will necessitate a gastroenterostomy in addition to the shunting procedure.

The Table represents a breakdown of the various types of procedures used in the series here reported. There were 60 patients with pathologically proved carcinomas of the pancreas who were operated on at the Swedish Hospital from 1947 through 1952.

Pathologically Proved Cases with Operation in Surgical Service of Swedish Hospital (1947-1952)

Proved surgical cases	60
Laparotomy only	21
Palliative procedures	
Cholecystostomy	2
Cholecystjejunostomy	11
Choledochojejunostomy	4
Choledochoduodenostomy	2
Gastroenterostomy	5
Whipple (carcinoma pancreas)	14
Whipple (ampullary carcinoma)	2
Other surgery	4

One might point with justifiable criticism to our 21 patients with laparotomy without any palliative procedure being done while the opportunity presented itself. Of these 21 patients, there were 10 with considerable fixation of surrounding structures from tumor invasion making any procedure hazardous. Many of the remainder unquestionably would have received some measure of benefit from a by-pass operation. Especially is this desirable when one considers the patient had already been exposed to exploration.

SUMMARY

An analysis of the treatment of carcinoma of the pancreas at the Swedish Hospital from 1947 through 1952 and those currently reported series in the literature makes us cognizant immediately of the disappointments and errors in judgment that occur. There is little evidence to show that we alter the natural history of carcinoma of the pancreas with surgery, and with rare exceptions this is a fatal disease. Radical resection for carcinoma of the pancreas should be undertaken in those patients in whom the carcinomatous process is limited strictly to the confines of the pancreas or the immediately adjacent duodenum. This will therefore include ampullary, lower bile duct, and duodenal carcinomas, which are favorable lesions for resection.

In those patients in whom the carcinoma has extended beyond the strict confines of the pancreas, a well-selected palliative procedure should be done when indicated.

REFERENCES

1. Whipple, A. O.; Parsons, W. B., and Mullins, C. R.: Treatment of Carcinoma of Ampulla of Vater, Ann. Surg. **102**:763, 1935.

2. Catell, R. B., and Pyrtek, L. J.: An Appraisal of Pancreatoduodenal Resection: A Follow-Up Study of Sixty-One Cases, Ann. Surg. **129**:840, 1949.

3. Miller, E. M., and Clagett, O. T.: Survival Five Years after Radical Pancreatoduodenectomy for Carcinoma of the Head of the Pancreas, Ann. Surg. **134**:1013, 1951.

4. Waugh, J. M.: Radical Resection of Head of Pancreas and Total Pancreatectomy, J. A. M. A. **137**:141, 1948.

5. McDermott, W. V., Jr.: A One Stage Pancreatoduodenectomy, Ann. Surg. **136**:1012, 1952.

6. Mathewson, C., Jr.: Indications for Pancreaticoduodenectomy, West. J. Surg. **60**:503, 1952.

7. Cole, W. H., and Reynolds, J. T.: Resection of Pancreas for Primary Carcinoma of Head of Pancreas and Ampulla of Vater, Surgery **18**:133, 1945.

8. Brunschwig, A.: Pancreatoduodenectomy a "Curative" Operation for Malignant Neoplasms in the Pancreatoduodenal Region, Ann. Surg. **136**:610-624, 1952.

EFFECT OF STREPTOKINASE-STREPTODORNASE ON PERITONEAL TALC ADHESIONS AND GRANULOMAS

Experimental Study

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STREPTOKINASE-streptodornase mixtures (Sk-Sd) have been used in a variety of clinical conditions characterized by the presence of purulent exudates or coagulated blood. The results obtained by local application or by instillation have been favorable in thoracic empyema, hemothorax and pleural effusions,* gangrene of the extremities,[9] infected sinus tracts,† osteomyelitis,[9] tuberculous meningitis and adenitis,‡ burns,[16] and miscellaneous soft tissue infections.§ The data suggest that streptokinase-streptodornase mixtures exert a double action. The streptokinase, in the presence of a serum component, lyses fibrin.‖ The streptodornase depolymerizes desoxyribonucleoprotein which accumulates in purulent exudates from the nuclei of dead cells.¶ The final result is a liquefaction of purulent or clotted material which is readily removed.

The present experiments were initiated to study the effects of Sk-Sd on peritoneal adhesions. It was assumed that these enzymes liquefy fibrinous and nucleoprotein exudates and, thus, that they might prevent peritoneal adhesions which develop from such exudates. Wright and his associates have reported that Sk-Sd prevented postoperative adhesions in the rabbit following scarification of the peritoneum.[23] In the present study talc was instilled into the peritoneal cavity of rats, and the favorable results obtained from the use of Sk-Sd corroborated those of Wright and his co-workers.

MATERIALS AND METHODS

White male and female rats ranging in weight from 200 to 350 gm. were used in all experiments. With the animals under ether anesthesia and with a nonsterile technique, the abdominal cavity was opened through a 3 cm. long right rectus muscle incision. Talcum veneticum, as

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* References 1 to 8.

† References 9 and 10.

‡ References 11 to 15.

§ References 17 and 18.

‖ References 19 and 20.

¶ References 21 and 22.

dry powder, was scattered throughout the peritoneal cavity. The abdomen was closed in two layers with continuous 00 nonabsorbable surgical (black silk) sutures, and collodion was applied to the wound.

All animals received 10 mg. of talcum per 100 gm. of body weight. To determine this optimal dose a previous experiment had been set up in which 5, 10, 20, 40, 60, and 100 mg. of talcum per 100 gm. of body weight was scattered into the peritoneal cavity of control and experimental animals. At the 10 mg. dose level the maximal difference was noted between those receiving Sk-Sd and those receiving saline.

The Sk-Sd # was dissolved in isotonic sodium chloride in an arbitrary concentration of 50,000 and 8,300 units of Sk and Sd, per milliliter, respectively. This solution was administered intraperitoneally in all experiments, in varying doses, as indicated below. Control rats were given saline intraperitoneally in quantities equivalent to those administered with Sk-Sd.

For all experiments the animals were paired, experimental and control.

Group I: Each of nine pairs of rats was killed at 2 to 3 day intervals up to 21 days after operation. At the time of laparotomy the treated rats received a single dose of 50,000 and 8,300 units of Sk-Sd per 100 gm. of body weight; the controls received saline.

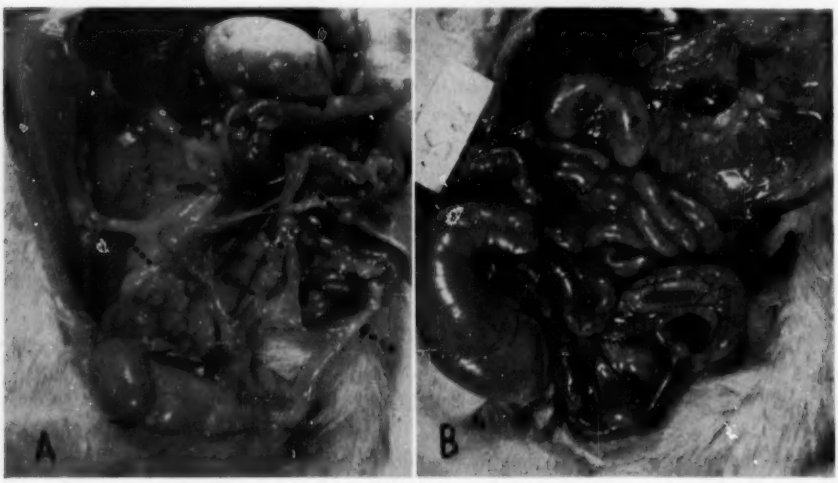

Fig. 1.—*A*, granulomas (——>) and adhesions (------>) in peritoneal cavity of rat after installation of talc and saline. *B*, absence of granulomas and adhesions in peritoneal cavity of rat after instillation of talc and streptokinase-streptodornase.

Group II: Six pairs of rats received a single dose of Sk-Sd or saline at the time of operation and were killed on the eighth postoperative day. The dose of the enzyme ranged from 25,000 Sk and 4,150 Sd to 150,000 Sk and 24,900 Sd units per 100 gm. of body weight.

Group III: Eight pairs of animals received a single dose at operation of 50,000 Sk and 8,300 Sd units per 100 gm. of body weight or saline. They were killed on the eighth day after the operation.

Group IV: Six pairs of rats received repeated intraperitoneal doses of Sk-Sd or saline over a period of 21 days, as shown in Table 4.

An additional five rats were laparotomized and closure was done in the same manner as in all the animals mentioned above. However, no talc, enzyme, or saline was instilled into the peritoneal cavity. Adhesions to the suture line were found in each of the five rats killed either on the 8th or the 21st postoperative day.

The streptokinase-streptodornase (Varidase; Lot No. 71089-232A) was supplied by Lederle Laboratories Division, American Cyanamid Company, New York.

At autopsy the number of granulomas, the number of intraperitoneal adhesions (exclusive of those in the suture line), and the number of adhesions to the suture line were recorded.

Segments of bowel and viscera with granulomas and adhesions were removed and placed in 4% formaldehyde fixative. The tissues were sectioned and stained with hematoxylin and eosin, toluidine blue, and Van Gieson's method.

TABLE 1.—*Number of Peritoneal Granulomas and Adhesions at Varying Time Intervals After Administration of Talc*

	Granulomas		Peritoneal Adhesions (Other Than to Suture Line)		Adhesions to Suture Line	
Day Killed	Controls	Sk-Sd Treated	Controls	Sk-Sd Treated	Controls	Sk-Sd Treated
2	3	2	1	0	1	1
4	46	5	0	0	1	1
6	20	1	1	0	1	1
8	19	0	1	0	1	0
10	49	26	4	3	0	1
13	52	10	3	1	1	1
15	38	11	4	3	1	1
18	27	31	0	1	1	1
21	43	25	3	0	1	2
Totals	297	111	17	8	8	9
Average	33	12.3	1.9	0.9	0.9	1

TABLE 2.—*Number of Peritoneal Adhesions and Granulomas Eight Days After Administration of Talc (Varying Doses of Sk-Sd)*

		Granulomas		Peritoneal Adhesions (Other Than to Suture Line)		Adhesions to Suture Line	
Rat No.	Doses of Sk-Sd Used per 100 Gm. Body Weight	Controls	Sk-Sd Treated	Controls	Sk-Sd Treated	Controls	Sk-Sd Treated
1	25,000/u Sk 4,150/u Sd	11	6	1	0	2	1
2	50,000 Sk 8,300 Sd	21	0	1	0	1	0
3	750,000 Sk 12,450 Sd	23	11	2	0	1	1
4	100,000 Sk 16,600 Sd	14	2	3	0	1	2
5	125,000 Sk 20,750 Sd	15	3	1	0	1	1
6	150,000 Sk 24,900 Sd	20	4	6	0	1	1
Total		104	26	14	—	7	6
Average		17.3	4.3	2.3	0	1.1	1

RESULTS

Table 1 shows the results of Group 1 in which the animals were killed at varying intervals up to 21 days after operation. The observations reveal that Sk-Sd depressed the formation of adhesions and granulomas for a period of eight days. The differences between the experimental and the control animals, in numbers both of adhesions and of granulomas, were marked. Beyond eight days the Sk-Sd treated animals still showed fewer adhesions and granulomas, but the difference was not so obvious. Adhesions to the suture line were of approximately equal number in treated and in untreated animals.

Varying the dose of Sk-Sd over a wide range had no effect on the outcome of the second experiment. In Table 2 it is seen that similar effective results were obtained with a minimal dose of 25,000 units of Sk and 4,150 units of Sd and a maximal dose of 150,000 units of Sk and 24,900 units of Sd.

To confirm the findings of the first two experiments, a third experiment was performed. In Table 3 the results revealed conclusively that Sk-Sd diminished the

TABLE 3.—*Number of Peritoneal Granulomas and Adhesions Eight Days After Administration of Talc*

	Granulomas		Peritoneal Adhesions (Other Than to Suture Line)		Adhesions to Suture Line	
Rat No.	Controls	Sk-Sd Treated	Controls	Sk-Sd Treated	Controls	Sk-Sd Treated
1	22	3	1	0	3	2
2	57	26	3	1	1	1
3	29	3	3	2	1	1
4	20	1	1	0	1	1
5	16	0	4	0	1	0
6	1	1	4	0	1	1
7	19	9	1	0	1	0
8	38	8	3	0	1	1
Total	202	51	20	3	10	7
Average	25.2	6.5	2.5	0.4	1.2	0.9

TABLE 4.—*Number of Peritoneal Adhesions and Granulomas 21 Days After Administration of Talc (Repeated Intraperitoneal Injection of Sk-Sd)*

	Granulomas		Peritoneal Adhesions (Other Than to Suture Line)		Adhesions to Suture Line	
Rat No.	Controls	Sk-Sd Treated	Controls	Sk-Sd Treated	Controls	Sk-Sd Treated
1*	53	3	4	0	2	1
2*	25	4	3	0	2	1
3*	29	12	2	0	1	1
4*	33	3	3	0	2	2
5†	28	3	3	0	1	2
6†	33	6	3	0	1	0
Total	201	31	18	0	9	7
Average	33.5	5.2	3	0	1.5	1.1

* Rats 1, 2, 3, and 4, received 50,000 units of Sk and 8,300 units of Sd every third day after operation for a total of seven injections.

† Rats 5 and 6 received 50,000 units of Sk and 8,300 units of Sd per 100 gm. of body weight every seventh day after operation for a total of three injections.

number of talc granulomas and adhesions (Figure). It was noteworthy that the number of adhesions to the suture line in both control and experimental rats was not significantly different.

In Table 4 are presented data of the animals receiving repeated injections of Sk-Sd and saline throughout a period of 21 days. In the treated animals the average number of granulomas was five, and no adhesions, exclusive of those in the suture line, were present. A comparison with Table 1 shows that with the administration of a single dose of Sk-Sd the average number of granulomas was 21, and in four of five animals intraperitoneal adhesions developed from 10 to 21 days after talc instillation.

Adhesions to the suture line were approximately the same in both control and experimental animals, despite repeated injections of Sk-Sd.

COMMENT

A single injection of Sk-Sd prevented almost completely the formation of intraperitoneal talc adhesions over a period of eight days, and multiple injections completely eliminated intraperitoneal talc adhesions throughout a period of 21 days. Of 20 animals treated with the enzyme, intraperitoneal adhesions developed in only 2, exclusive of those in the suture line (Groups II, III, and IV). In 20 control rats adhesions were present in every animal. Similarly, in animals treated with Sk-Sd the number of granulomas was diminished markedly, as compared with controls which did not receive the enzyme. The average number of granulomas for all treated rats was 7.5 as compared with an average of 27.7 for all controls.

The results of these experiments also demonstrated that Sk-Sd was optimally effective for a period of eight days. The efficacy of the drug was prolonged by repeating the injections at intervals of less than eight days.

The favorable result within the first eight days after administration of Sk-Sd might have been due to one or more factors. Liquefaction of the early exudates induced by the talc may have facilitated absorption of fibrin, of nucleoproteins, and also of some of the talc granules. As a result, the formation of granulomas and adhesions was delayed. After eight days the remaining talc induced the usual granulomatous and fibrous reaction. Liquefaction of the early exudates might also have permitted the ready removal of bacteria, which most likely gained entrance to the peritoneal cavity during the operative procedure and which might have enhanced the formation of granulomas and adhesions. A sterile technique was not employed in these animals. Johnson [24] has reported a more effective phagocytosis and early sterilization of the affected locus following liquefaction of infected coagula by Sk-Sd. Lastly, it was possible that antienzymes developed after the eighth day and prevented the Sk-Sd from working. Hazlehurst [25] has shown that antibodies to these enzymes appeared from 9 to 42 days after a single injection. The available data, however, have indicated that Sk-Sd is quickly destroyed or inactivated. In the present experiments, therefore, the development of antienzymes would not be likely.

The minimal effective dose was not determined nor was the toxic dose. With a quantity as small as 25,000 units of Sk and 4,150 units of Sd the formation of granulomas and adhesions was prevented as effectively as with a dose six-fold greater.

The development of adhesions to the suture line in both Sk-Sd treated and control rats is difficult to explain. There were, however, extrinsic factors which might have vitiated the action of Sk-Sd at the suture line in the experimental animals. First, the sutures were of nonabsorbable surgical (silk) suture material and constituted a persistent irritating agent. Second, healing of the incision must be accomplished on a basis of fibrinous exudate. Sk-Sd might delay repair between cut surfaces, but it would be unable to prevent it, for the stimulus to fibrosis persists. The talc granules did not present such a continuing stimulus for repair because they were slowly removed from the abdominal cavity. It was also quite likely that the

ventral position of the rat viscera facilitated the development of adhesions in the suture line by constant pressure of the omentum and the intestines against the wound.

Histological examination of the granulomas and adhesions revealed no differences between the experimental and the control animals. The initial reaction to the talc was one of acute localized inflammation and necrosis. Within four to six days giant cells and collagen fibrils appeared and increased in number. At 15 days after talc administration the granulomas decreased in size, collagen began to disappear, and the granulomas showed a loose structure. These observations indicated that Sk-Sd exerted its action before morphological reactions were visible.

SUMMARY

The intraperitoneal instillation of streptokinase-streptodornase (Sk-Sd) prevented the formation of adhesions and diminished the number of granulomas induced by talc in the peritoneal cavity of rats. The enzyme was clearly effective for a period of eight days. Repeated injections of Sk-Sd prolonged the effective action of the enzyme for 21 days. Sk-Sd was efficacious over a wide range of doses, and no toxic reactions were seen with the highest dose used. Sk-Sd had no influence on the adhesions which developed in the suture line.

REFERENCES

1. Gaensler, E. A., and Strieder, J. W.: Streptokinase-Streptodornase in the Treatment of Extrapleural Hematoma Complicating Extrapleural Pneumothorax, Am. Rev. Tuberc. **63**:547 (May) 1951.

2. Gauld, B. G., and Harold, J. T.: Massive Hemothorax in Artificial Pneumothorax Treated with Streptokinase, Brit. J. Tuber. **44**:77 (July) 1950.

3. Goldman, A.: Medical and Surgical Decortication of the Pleura in Chronic Pleural Effusion, J. Lab. & Clin. Med. **36**:827 (Nov.) 1950.

4. Read, C. T., and Berry, F. B.: The Utilization of Streptokinase-Streptodornase in a Patient with Hemopneumothorax and a Patient with Post-Pneumonectomy Sanguineous Coagulum, J. Thoracic Surg. **20**:384 (Sept.) 1950.

5. Sherry, S.; Tillett, W. S., and Read, C. T.: The Use of Streptokinase-Streptodornase in the Treatment of Hemothorax, J. Thoracic Surg. **20**:393 (Sept.) 1950.

6. Tillett, W. S., and Sherry, S.: The Effect in Patients of Streptococcal Fibrinolysin (Streptokinase) and Streptococcal Desoxyribonuclease on Fibrinous, Purulent, and Sanguineous Pleural Exudations, J. Clin. Invest. **28**:173 (Jan.) 1949.

7. Tillett, W. S.; Sherry, S., and Read, C. T.: The Use of Streptokinase-Streptodornase in the Treatment of Post-Pneumonic Empyema, J. Thoracic Surg. **21**:275 (March) 1951.

8. Tillett, W. S.; Sherry, S., and Read, C. T.: The Use of Streptokinase and Streptodornase in the Treatment of Chronic Empyema, J. Thoracic Surg. **21**:325 (April) 1951.

9. Miller, J. M.; Ginsberg, M.; Lipin, R. J., and Long, P. H.: Clinical Experience with Streptokinase and Streptodornase, J. A. M. A. **145**:620 (March) 1951.

10. Sherry, S.: The Local Use of Streptokinase-Streptodornase in Refractory Chronic Draining Sinuses, Forum on Fundamental Surgical Problems: Clinical Congress of the American College of Surgeons, Philadelphia, W. B. Saunders Company, 1951.

11. Cathie, I. A. B.: Streptomycin-Streptokinase Treatment of Tuberculous Meningitis, Lancet **1**:441 (March) 1949.

12. Cathie, I. A. B., and MacFarlane, J. C. W.: Adjuvants to Streptomycin in Treating Tuberculous Meningitis in Children, Lancet **2**:784 (Dec.) 1950.

13. Hazlehurst, G. N.: Streptokinase-Streptodornase in the Treatment of Suppurative Tuberculous Adenitis, Forum on Fundamental Surgical Problems: Clinical Congress of the American College of Surgeons, Philadelphia, W. B. Saunders Company, 1951.

14. McSweeney, C. J.: The Treatment of Tuberculous Meningitis, Irish J. M. Sc. **6**:418 (Sept.) 1950.

15. Williams, S., and Babeley, P. L.: The Use of Streptokinase in the Treatment of Tuberculous Meningitis, M. J. Australia **2**:690 (Nov.) 1950.

16. Tillett, W. S.: Use of Streptokinase-Streptodornase in Burns: A Symposium on Burns, Nov. 2-4, 1950, Washington, D. C., National Research Council, 1951; abstracted, Lancet **2**:635 (Nov. 25) 1950.

17. Tillett, W. S.; Sherry, S.; Christensen, L. R.; Johnson, A. J., and Hazlehurst, G. N.: Streptococcal Enzymatic Débridement, Ann. Surg. **131**:12 (Jan.) 1950.

18. Wright, L. T.; Smith, D.; Rothman, M.; Metzger, W. I., and Quash, E. T.: The Use of Streptokinase-Streptodornase in Certain Surgical Conditions, J. Internat. Coll. Surgeons **15**:286 (March) 1951.

19. Christensen, L. R.: Streptococcal Fibrinolysis: A Proteolytic Reaction Due to a Serum Enzyme Activated by Streptococcal Fibrinolysin, J. Gen. Physiol. **28**:363 (March) 1945.

20. Milstone, H.: A Factor in Normal Human Blood Which Participates in Streptococcal Fibrinolysis, J. Immunol. **42**:109 (Oct.) 1941.

21. Sherry, S., and Goeller, J. P.: The Extent of the Enzymatic Degradation of Desoxyribonucleic Acid (DNA) in Purulent Exudates by Streptodornase, J. Clin. Invest. **29**:1588 (Dec.) 1950.

22. Tillett, W. S.; Sherry, S., and Christensen, L. R.: Streptococcal Desoxyribonuclease: Significance in Lysis of Purulent Exudates and Production by Strains of Hemolytic Streptococci, Proc. Soc. Exper. Biol. & Med. **68**:184 (May) 1948.

23. Wright, L. T.; Smith, D. H.; Rothman, M.; Quash, E. T., and Metzger, W. I.: Prevention of Postoperative Adhesions in Rabbits with Streptococcal Metabolites, Proc. Soc. Exper. Biol. & Med. **75**:602 (Nov.) 1950.

24. Johnson, A. J.: Cytological Studies in Association with Local Injections of Streptokinase-Streptodornase into Patients, J. Clin. Invest. **29**:1376 (Oct.) 1950.

25. Hazlehurst, G. N.: Anti (Streptococcal) Desoxyribonuclease Occurrence in the Sera of Patients Treated with Streptococcal Concentrates Containing Streptodornase, J. Immunol. **65**:85 (July) 1950.

PROTEIN NUTRITION IN SURGICAL PATIENTS

I. A Time Factor in the Protein-Sparing Action of Dextrose in Parenteral Feeding

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DETROIT

SATISFACTORY preoperative and postoperative treatment of the surgical patient must include adequate nutrition. When the patient cannot or will not eat, the parenteral feedings he receives are often woefully lacking in calories, protein content, or both. Because the quantity of fluid required for intravenous alimentation has imposed severe limitations on the quantity of nutritive substances which can be administered by this route, it is mandatory that these substances be given in such a manner as to provide for their maximum utilization.

The absence of any mechanism for storage of a large amount of available protein in the body makes provision of exogenous protein imperative. However, it has been shown that when proteins or amino acids are supplied without sufficient calories, more are used by the body for energy than for tissue formation. A protein hydrolysate given intravenously can supply both the essential and the nonessential amino acids simultaneously and without regard to differential digestion rates. Under these conditions must carbohydrate be present simultaneously or is it required only to provide an adequate total caloric intake?

This paper presents the results of experiments designed to investigate the time factor in protein synthesis in the postoperative patient fed exclusively by intravenous injections of dextrose and protein hydrolysate.

METHODS

In the course of the investigation 18 postoperative patients were studied; of these 12 had gastric operations, 2 had partial colectomies, and 4 had cholecystectomies. The patients were divided into two groups. The first group included 10 patients who received dextrose simultaneously with a protein hydrolysate (Travamin). From 50 to 200 ml. of 50% dextrose solution was added directly to 2 liters of 5% protein hydrolysate in 5% dextrose prior to administration of the latter. As necessary, a measured amount of hydrolysate was removed to permit inclusion of the dextrose and the appropriate corrections made in the calculated intake. For this reason the patients in Group I received somewhat smaller quantities of nitrogen daily than did those in Group II. Such additional calories as were required were given as 20% dextrose solutions intravenously, either alternately with the 2 liters of hydrolysate or immediately after them.

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The second group consisted of eight patients who were given dextrose (20% solution) four hours after the protein infusion was completed. The protein hydrolysate was given to these patients in water. The infusions were well tolerated by both groups. Transient nausea was occasionally noted when the material was given rapidly but was usually stopped by slowing down the rate of administration. Patients in both groups were studied for periods of two to four days.

The basal calories required for each patient were determined from the DuBois charts on the basis of height, weight, age, and sex. A slide rule calibrated on the basis of the DuBois chart permits rapid calculation of the basal metabolic requirement. Approximately 30% more calories are required for bed activity. Inasmuch as all the persons included in this study were bed patients in the hospital, and because the calories which could be given to patients in Group II were limited, we arbitrarily regarded the caloric requirement of all patients to be their basal requirement plus 30%. None of the patients were clinically considered to have abnormal thyroid function. The caloric balance was calculated as the difference between the calculated caloric requirement and the calories given. Owing to the fact that caloric restriction alone frequently results in marked negative nitrogen balance, only those patients who were within 300 Cal. of their estimated requirement were included in this study. Preliminary studies of our own indicated that at caloric intakes below this level the effects of caloric restriction were superimposed on the effects of protein-carbohydrate separation.

Urine was collected for 24-hour periods and analyzed for total nitrogen content. When a Levin or Wagensteen tube was used, the drainage was also collected daily and analyzed. Collections were followed closely, and any doubtful cases were discarded, as were those on whom collections were incomplete. Water was allowed ad libitum, but nothing else was given by mouth during the period of the experiment. The hydrolysate, urine, and drainage were analyzed for nitrogen by the macro-Kjeldahl procedure. Aliquots of the hydrolysate taken from different lots over a period of a year were remarkably constant. The total nitrogen intake and output was then calculated and the difference regarded as the nitrogen balance.

RESULTS

As seen in Table 1 the patients in Group I had an average daily nitrogen balance of —3.11 gm. of nitrogen, with a range of values from —8.52 to +2.18 gm. of nitrogen. Eight of the 10 patients lost less than 4.5 gm. of nitrogen daily, and 2 were in positive balance. The deficient caloric intake and/or failure to provide sufficient nitrogen to fulfill the need of the patient appears to be the reason for the inability to keep these patients in positive balance. The average caloric intake was 143 Cal. below the basal requirement plus 30%. A scattergraph of these data shows a roughly direct correlation between nitrogen balance and percent of caloric requirement infused, with the exception of Cases 7 and 27, and is in agreement with the results obtained by Rice.[11]

The data obtained on the cases in Group II are given in Table 2. The average daily nitrogen balance in these patients was —8.50 gm. of nitrogen. The values ranged from —4.17 to —11.76 gm., with only one of the eight patients losing less than 4.5 gm. of nitrogen daily and none in positive balance. The average caloric

intake in this group was somewhat better than in Group I, being exactly the basal caloric requirement plus 30%. A scattergraph of these data, however, shows no correlation between caloric intake and nitrogen balance, further demonstrating that the metabolism of amino acids in man is too rapid to be influenced by calories provided four hours later.

TABLE 1.—*Nitrogen Balance in Patients Receiving Dextrose and Protein Hydrolysate Simultaneously*

Case	Avg. Daily Caloric Balance, Cal.	Avg. Daily Nitrogen Intake, Gm.	Avg. Daily Nitrogen Balance, Gm.	Operation
1	— 260	11.19	— 4.49	Gastrojejunal colic fistula
2	— 260	9.95	— 2.07	Subtotal gastric resection
3	— 80	11.81	+ 0.36	Mikulicz colostomy for ca. of colon
7	— 200	10.57	— 8.23	Cholecystectomy and appendectomy (dermal ca.)
8	— 200	10.57	+ 2.18	Gastroenterostomy with vagotomy and appendectomy
11	— 60	9.95	— 2.35	Anterior gastrojejunostomy for recurrent ca.
12	— 180	9.95	— 2.30	Cholecystectomy
13	— 60	10.57	— 2.03	Gastroenterostomy with vagotomy
15	— 200	10.57	— 3.67	Cholecystectomy
27	+ 70	11.19	— 8.52	Colon resection for ca.
Average	— 143	10.63	— 3.11	

TABLE 2.—*Nitrogen Balance in Patients Receiving Dextrose Four Hours After Receiving Protein Hydrolysate*

Case	Avg. Daily Caloric Balance, Cal.	Avg. Daily Nitrogen Intake, Gm.	Avg. Daily Nitrogen Balance, Gm.	Operation
9	0	12.44	— 9.11	Gastrojejunostomy
24	— 150	12.44	— 11.76	Subtotal gastric resection with gastrojejunostomy
25	— 80	12.44	— 4.17	Cholecystectomy and appendectomy
26	— 230	12.44	— 11.61	Gastric resection
28	+ 240	12.44	— 11.27	Gastric resection
29	+ 260	12.44	— 5.55	Gastric resection
30	— 120	12.44	— 7.30	Gastrectomy with vagotomy
31	+ 80	12.44	— 7.25	Gastroenterostomy with vagotomy
Average	0	12.44	— 8.50	

COMMENT

The work of Ellison [3] indicating that the utilization of protein is related to the total caloric intake has been followed by attempts to find a satisfactory source of these requisite calories. Rice and his associates [12] have used ethyl alcohol in conjunction with dextrose and amino acids. Van Itallie and his associates,[14] Mann and his co-workers,[9] and others have added fat to parenterally administered solutions in an effort to obtain a high caloric intake in a satisfactory volume of fluid which would result in protein-sparing and nitrogen retention. However, adequate calories per se are not the only factor exerting a protein-sparing action. Larson and Chiakoff [17] reported, in 1937, that the protein-sparing effect of carbohydrate

depended upon a time factor, and unless the two substances were given almost simultaneously the protein was used for energy or in some way dissipated without utilization for growth or maintainance. Cuthbertson and Munro [2] drew the same conclusion, based on the results of oral-feeding experiments. Elman [4] described one case in which this was true of intravenous feeding. Kayser and Tallquist, feeding isodynamic quantities of carbohydrate and fat, found that, while carbohydrate enhanced nitrogen storage, fat tended to interfere with it (Sherman, 1941 [13]). Cuthbertson and Munro [*] also found that separation of fat from protein in the diet did not result in nitrogen loss, although separation of the carbohydrate from the protein in the diet resulted in negative balances on adequate caloric intakes, a conclusion confirmed by others.[8] Geiger [5] has suggested that inasmuch as it has been shown that all the essential amino acids must be present simultaneously for formation of new protein [6] it is probable that the simultaneous presence of the precursors of the nonessential amino acids is also necessary.

The results of the experiments described here show that carbohydrate increases nitrogen retention in postoperative patients when intravenous protein hydrolysate is the only source of nitrogen and all the amino acids are supplied simultaneously. That this result is not due to calories alone is demonstrated by the observation that the patients did not exhibit the same nitrogen retention when there was a four-hour interval between the protein and dextrose feeding that was exhibited when the two substances were given simultaneously, although they received the same caloric intake. Thus it appears not only that dextrose is necessary for calories or as a precursor of nonessential amino acids but also that the simultaneous metabolism of exogenous dextrose is necessary for nitrogen retention and protein synthesis when the diet does not contain excessive quantities of protein.

SUMMARY

Ten postoperative patients receiving intravenously administered dextrose and protein hydrolysate simultaneously had an average daily nitrogen balance of —3.11 gm. of nitrogen, with two patients in positive balance. Eight of the 10 lost less than 4.5 gm. of nitrogen daily. Eight similar patients receiving intravenous dextrose and protein hydrolysate in the same quantity, but separated by a four-hour interval, had an average daily nitrogen balance of —8.50 gm. of nitrogen and only one patient lost less than 4.5 gm. of nitrogen daily. It is concluded that in patients maintained by intravenous feeding exclusively, the protein-sparing action of dextrose depends on its infusion simultaneously with amino acids, entirely apart from its caloric effect.

REFERENCES

1. Cuthbertson, D. P., and Munro, H. N.: Protein Saving Effects of Carbohydrate and Fat when Superimposed on a Diet Adequate for Maintenance, Biochem. J. **31**:694, 1937.

2. Cuthbertson, D. P., and Munro, H. N.: The Relationship of Carbohydrate Metabolism to Protein Metabolism, Biochem. J. **33**:128, 1939.

3. Ellison, E. H.; McCleary, R. S.; Zollinger, R. M., and Case, C. T.: The Influence of Caloric Intake upon the Fate of Parenteral Nitrogen, Surgery. **26**:374, 1949.

4. Elman, R.: Time Factor in Retention of Nitrogen After Intravenous Injection of a Mixture of Amino Acids, Proc. Soc. Exper. Biol. & Med. **40**:484, 1939.

*References 1 and 10.

5. Geiger, E.: The Importance of the Time Element in Feeding of Growing Rats, Science **108**:42, 1948.

6. Geiger, E.. The Role of the Time Factor in Protein Synthesis, Science **111**:594, 1950.

7. Larson, P. S., and Chiakoff, I. L.: The Influence of Carbohydrate on Nitrogen Metabolism in the Normal Nutritional State, J. Nutrition **13**:287, 1937.

8. Lathe, G. H., and Peters, R. A.: The Protein Sparing Effect of Carbohydrate in Normal and Burned Rats, Quart. J. Exper. Physiol. **35**:157, 1949.

9. Mann, G. V.; Geyer, R. P.; Watkin, D. M., and Stare, F. J.: Parenteral Nutrition: IX. Fat Emulsion for Intravenous Nutrition in Man, J. Lab. & Clin. Med. **34**:689, 1949.

10. Munro, H. N.: Relationship of Carbohydrate Metabolism to Protein Metabolism: III. Further Observations on Time of Carbohydrate Ingestion as a Factor in Protein Utilization in the Adult Rat, J. Nutrition **39**:375, 1949.

11. Rice, C. O.; Treloar, A. E., and Stricker, J. H.: Parenteral Nutrition in Surgery, Arch. Surg. **61**:977, 1950.

12. Rice, C. O.; Orr, B., and Enquist, L.: Parenteral Nutrition in the Surgical Patient Provided from Glucose, Amino Acids, and Alcohol, Ann. Surg. **131**:289, 1950.

13. Sherman, H. C.: Chemistry of Food and Nutrition, Ed. 6, New York, The Macmillan Co., 1941.

14. Van Itallie, T. B.; Waddell, W. R.; Geyer, R. P., and Stare, F. J.: Clinical Use of Fat Injected Intravenously, A. M. A. Arch. Int. Med. **89**:353, 1952.

SURGICAL SIGNIFICANCE OF THE MARGINAL MANDIBULAR BRANCH OF THE FACIAL NERVE

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INTEREST tends to be lost in the fundamental science of anatomy in this surgical decade of wider excision and physicochemical problems. This subject is anatomical. It is the result of several years of clinical observation supported by the written reports of other authors.

THE PROBLEM

In a recent report Woodhall [12] warns against accidental division of the spinal accessory nerve during minor operations in the posterior triangle of the neck. Such a mishap results in a paralysis of the trapezius muscle. In the upper neck, incision and dissection for protean entities frequently results in a paralysis of the corner of the mouth, or the depressor anguli oris muscle, on the side of operation. Division of the marginal mandibular branch of the facial nerve is the cause of this bothersome cosmetic deformity (Fig. 1). It may occur after removal of a lymph node or a simple branchiogenic cyst. The significance of this nerve is not only cosmetic; once its position is made clear, it aids in rapid identification of the main trunk of the facial nerve, so essential in parotid surgery. Its proper recognition is an important step in head and neck operations.

SURGICAL ANATOMY

While neck dissections are being performed, the inferior pole (or tail) of the parotid gland is cut across. As a constant finding a medium-sized vein was seen emerging from just beneath the central portion of the gland at its most inferior point. This structure was later identified as the posterior facial vein, which arises superior to the parotid and travels downward through its substance but is unattached to the gland at its inferior pole. Frequently running on the surface of the vein, at times a few millimeters anterior to it, or occasionally crossing it diagonally as it emerges from beneath the gland, is the marginal mandibular branch of the facial nerve. The position of these two structures at this point is in the neck, below the angle of the mandible, and not on the cheek (Figs. 2 and 3).

The branch travels downward with the vein for 1 or 2 cm. before moving anteriorly and dividing into a cervical descending ramus, which supplies a portion of the platysma of the upper neck, and the mandibular ramus, which continues forward beneath the platysma and almost parallel to the mandible for several centimeters, before coursing upward to supply the motor innervation of the lower lip. By tracing the branch upward (proximal) for 2 or 3 cm. the main trunk of the facial nerve may be reached. Identification of the marginal branch is aided by the invariable position of the posterior facial vein. In numerous dissections this vein was found in a constant location.

Fig. 1.—Patient showing loss of motor innervation of half of the lower lip following surgery performed for the removal of a tumor in the upper neck. The line of incision is outlined.

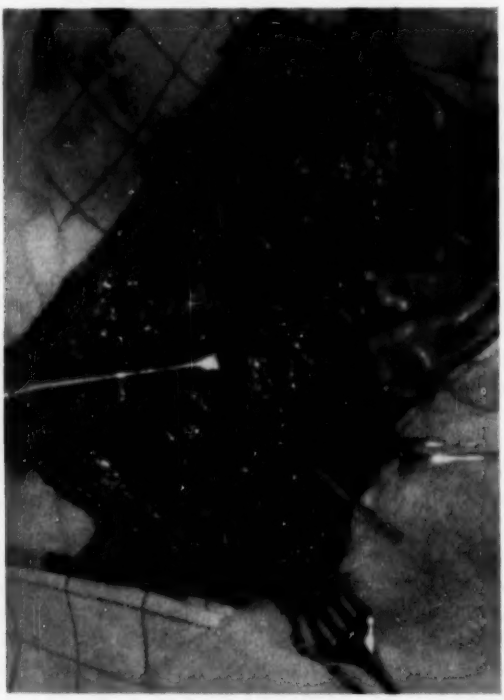

Fig. 2.—Actual operating-room view after total parotidectomy, revealing branches of the facial nerve. In this case the mandibular branch runs downward on top of the posterior facial nerve.

Byars [8] has recently written on this anatomical relationship, and full credit must be given to him as the first to report it in the surgical literature. He states that in no instance has this relationship "let him down," but he warns against confusing the external jugular vein with the posterior facial vein. The former travels on top of the sternocleidomastoid muscle, whereas the latter courses deep to it.

COMMENT

Danger of inadvertent injury to the marginal mandibular branch is present in almost any surgical procedure performed in the upper neck. When incision and dissection approach the critical area below the angle of the mandible, where nerve and vein are close, it is well to identify the mandibular branch first, trace it for-

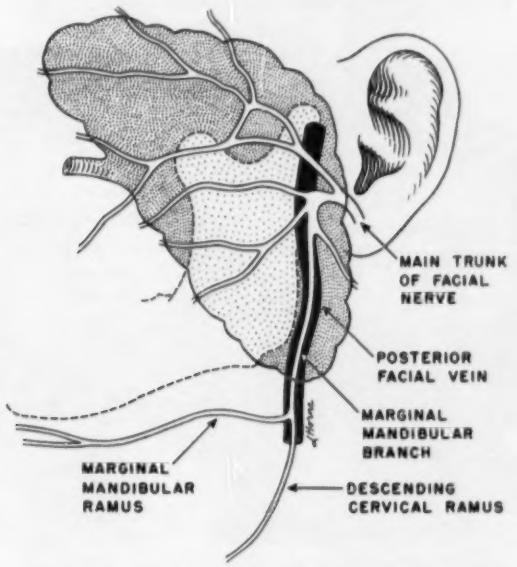

Fig. 3.—Artist's drawing of Figure 2. The parotid gland has been superimposed. Note the critical area at the inferior tip of the gland with vein and nerve emerging from underneath. This relationship is below the angle of the mandible and in the neck.

ward as it courses deep to the platysma muscle and reflect it away from the surgical field. This is especially important in minor operations in which resulting paralysis is hardly compatible with the procedure performed. Operations performed further anteriorly may involve the distal portion of the nerve because in many instances it does not course above the mandibular margin for 3 or 4 cm. When the distal portion is composed of several smaller branches, as is frequently the case, it becomes increasingly difficult to preserve them all. When some (one or more) are preserved, the resulting deformity is minimal because of anastomoses of the terminal endings with other (buccal) rami * (Fig. 4).

Lahey [5] states that it is impossible in performing a radical dissection of the neck to avoid injury to this nerve, especially if all nodes in the region beneath the

*Martin,[8] and McCormack, and others.[9]

angle of the mandible are removed. However, preliminary identification of the nerve first would in most instances prevent injury to it and does not impair thorough dissection. This assertion is supported by the studies of Martin,[7] who makes a special point of identifying this nerve while performing neck dissections. The belief that section of the tail of the parotid gland is responsible for partial paralysis of the lip is true in so far as the surgeon in dividing the parotid at this point also clamps and divides the posterior facial vein, a step which frequently will divide the mandibular branch near its point of origin.

Surgery of parotid tumors has come a long way since Sir Frederick Treves's [11] statement: "It follows from the complex relations of the parotid that its entire removal as a surgical procedure is an anatomical impossibility." Yet the technique of performing a parotidectomy with visualization of one or more branches of the

Fig. 4.—Result following right hemithyroidectomy and right radical neck dissection performed in continuity for carcinoma of the thyroid with cervical lymph node metastasis. The marginal mandibular ramus divided anteriorly into several filaments, but with one preserved motor innervation of the lower lip was not lost. The lines of incision are shown.

facial nerve was slow in gaining acceptance. The high number of recurrences † following excision of parotid tumors by other methods proves the value of facial nerve dissection. There are many techniques described by numerous authors.‡ One method [3] is to identify the main trunk of the facial nerve by tracing the marginal mandibular branch upward. As was previously stated, the mandibular branch is located by its constant association with the posterior facial vein as that structure emerges from beneath the lowermost tip of the parotid. When the dissection is started at this point a broad segment of the nerve is easily visualized close to the gland. This not only limits the extent of dissection, but is of comfort to the sur-

† Kidd,[4]; Marshall and Miles,[6] and McCune.[10]

‡ Adson and Ott [1]; Bailey [2]; Kidd [4]; Marshall and Miles [6]; Martin and McCune.[10]

geon in that he isolates a major portion of the nerve early in the operation. All or part of the gland may then be removed with full visualization of one or more facial nerve branches (Fig. 5).

Fig. 5.—Postoperative result following total parotidectomy for a recurrent mixed tumor. The gland was removed by identifying the mandibular branch first and then dissecting upward to reach the main trunk of the facial nerve. The type of incision used is outlined.

SUMMARY

The marginal mandibular branch of the facial nerve can be divided accidentally during minor surgical procedures in the upper neck. It may be identified at the lowermost tip of the parotid gland by the accompanying posterior facial vein. Awareness of this relationship and of its anterior branches will prevent paralysis

of half of the lower lip. By identifying this branch first and tracing it upward to the main trunk of the facial nerve, parotidectomy can be performed under visualization of the branches of the facial nerve.

450 Sutter St.

BIBLIOGRAPHY

1. Adson, A. W., and Ott, W. O.: Preservation of the Facial Nerve in the Radical Treatment of Parotid Tumors, Arch. Surg. **6**:739-747 (June) 1923.

2. Bailey, H.: The Surgical Anatomy of the Parotid Gland, Brit. M. J. **2**:245-248 (July) 1948.

3. Byars, L. T.: Preservation of the Facial Nerve in Operations for Benign Conditions of the Parotid Area, Ann. Surg. **136**:412-421 (Sept.) 1952.

4. Kidd, H. A.: Complete Excision of the Parotid Gland with Preservation of the Facial Nerve, Brit. M. J. **1**:989-992 (April 29) 1950.

5. Lahey, F. H.: Radical Dissection of the Neck, S. Clin. North America, **29**:631-641 (June) 1949.

6. Marshall, S. F., and Miles, G. O: Tumors of Submaxillary and Parotid Gland Areas, S. Clin. North America, **27**:501-516 (June) 1947.

7. Martin, H. E.: Del Valle, B.; Ehrlich, H., and Cahan, W. G.: Neck Dissection, Cancer **4**:441-499 (May) 1951.

8. Martin, H. E.: The Operative Removal of Tumors of the Parotid Salivary Glands, Surgery **51**:670-682 (May) 1952.

9. McCormack, L. J.; Cauldwell, E. W., and Anson, B. J.: The Surgical Anatomy of the Facial Nerve, Surg. Gynec. & Obst. **80**:620-635 (June) 1945.

10. McCune, W. S.: Total Parotidectomy in Tumors of the Parotid Gland, A.M.A. Arch. Surg. **62**:715-723 (May) 1951.

11. Treves, F.: Surgical Applied Anatomy, Ed. 4, London, Cassell & Co., Ltd., 1902.

12. Woodhall, B.: Trapezius Paralysis Following Minor Surgical Procedures in the Posterior Cervical Triangle: Results Following Cranial Nerve Suture, Ann. Surg. **136**:375-380 (Sept.) 1952.

RETROPUBIC APPROACH TO BLADDER NECK RESECTION IN CHILDREN

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CONTRACTURE of the vesical neck is one of the commonest congenital anomalies of the genitourinary tract. The highest incidence occurs in children below 6 years of age, but, since many cases are either not detected or the childhood symptoms not recognized until the second or third decade, the true incidence is uncertain.

These symptoms are often identical with those of prostatism and other forms of lower urinary tract obstruction found in the adult. Frequently they are undetected or ignored by the physician until back pressure has caused dilatation of the upper urinary tract to an advanced and sometimes irreversible degree. Eneuresis resistent to psychiatric management or repeated episodes of urinary tract infection refractory to symptomatic treatment may on proper investigation prove to be due to an obstructive uropathy responsive only to surgical correction. Occasionally, a patient is referred to the urologist for such late manifestations of the disease as an abdominal mass or the uremic state.

The diagnosis of lower urinary tract obstruction of any variety can be made most readily by a determination of the urinary residual, a simple office procedure. Campbell [1] considers any residual above 15 cc. significant.

Treatment has been almost exclusively surgical, as dilatation of the bladder neck by sounds or bougies has not proved to be of lasting value. Beneficial results in two of our cases lasted only two weeks. The nonoperative treatment is also impracticable because in male children it requires general anesthesia. We feel that one operation is preferable to a lifetime of instrumentation under anesthesia.

Originally the cold punch was used in transurethral resection, but at present the infant resectoscope enjoys the most popularity. Unfortunately, not all hospitals have such an instrument. Moreover, transurethral resection in children has certain limitations. All the pitfalls of transurethral resection in the adult are magnified many times in these small patients, since the infant resectoscope affords poor visability and makes for difficulty in securing adequate hemostasis. The dangers of urinary extravasation and rectal perforation are real, as the tissue between the rectal mucosa

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and bladder neck is, as Campbell [2] points out, "thin as cigarette paper." It is extremely difficult to determine accurately the proper amount of tissue to resect in order to secure an adequate vesical outlet. Even as experienced a pediatric urologist as Campbell [1] has had to perform as many as three transurethral resections of the bladder neck in the same patient before obtaining a satisfactory result. In infants an external urethrotomy may be required to accommodate even the small resectoscope. Urinary incontinence, while rare in the hands of an experienced resectionist, is a tragedy when it occurs. Severe, often intractable, urethral strictures may occur later on in life. This complication has been observed by one of us in adults who have had urethral instrumentation in childhood.

The suprapubic approach has the disadvantage of inadequate exposure of the bladder neck area, with the result that less tissue can be resected.

The rapid growth in popularity in this country of Millen's retropubic prostatectomy has encouraged others to employ this approach in bladder neck resections. Burns [3] and Lich and Maurer [4] and Hand [5] have modified the original Millen technique by employing a longitudinal incision in the prostatic capsule, which can be extended distally as far as the verumontanum, enabling the entire prostatic urethra to be visualized. Congenital urethral valves can be resected readily by this approach, and by carrying the incision upward the bladder can be opened widely to correct any pathology within. If prolonged obstruction has resulted in upper tract pathology, a cystotomy can be performed by a stab incision through the anterior bladder wall.

To date we have been able to find a total of 26 reported cases (Burns, 20 cases; Lich and Maurer, 5 cases, and Hand, 1 case). There are probably many more in the voluminous literature on retropubic prostatectomy as well as many that have not been reported. Although the 26 cases were not described in detail, no fatalities, serious complications, or operative failures were noted. To this small series we add six cases of our own.

Our youngest patient was a 1-year-old infant; the oldest, a 13-year-old boy. Two patients were 2½ years of age, and the remaining two were 4 and 7 years old. Our six cases illustrated the full range of symptoms resulting from vesical neck obstruction and an elevated urinary residual. In two patients there were lower urinary tract symptoms: hematuria, pyuria, dysuria, and suprapubic pain. One of them had costovertebral angle tenderness, a urosepsis severe enough to cause a convulsion, and a septic temperature refractory to all therapy until bladder drainage was instituted. Two patients had complete retention. One was the 12-month-old infant. The other presented a bladder palpable at the umbilicus, which had been diagnosed an abdominal tumor at another hospital. The remaining two (ages 7 and 13) had histories of eneuresis and diurnal dribbling with stress incontinence since infancy.

The urinary residuals varied from peaks of 250 and 350 cc. in the patients having urinary retention to lows of 30 and 75 cc. in the eneuretics. Residuals of 50 to 100 cc. and 75 to 250 cc. were found in the two patients with lower tract symptoms. Those having values of less than 100 cc. were given a trial of nonoperative treatment. The residuals decreased to 35 and 5 cc. after sounding, but in two weeks they had returned to their previous high levels.

Preoperative cystoscopy revealed in each of these a concentric, collar-like, crenated contracture of the bladder neck and a sharp drop of the urethra between the verumontanum and the raised vesical outlet. Lower tract obstruction, as evi-

denced by trigonal hypertrophy with *bas fond* formation, trabeculation, cellule, saccule, and diverticula formation, was present in variable degrees. These findings were substantiated at the time of operation.

Cystography and intravenous pyelography, important in detecting upper urinary tract involvement as well as bladder pathology, showed diverticula almost equal in size to the bladder in two cases and a small one in a third. In no case was ureteral reflux demonstrated.

Cystometry serves to rule out neurogenic disorders but is difficult to perform and gives unreliable results in infants and young children. It was normal in the two cases in which it was performed.

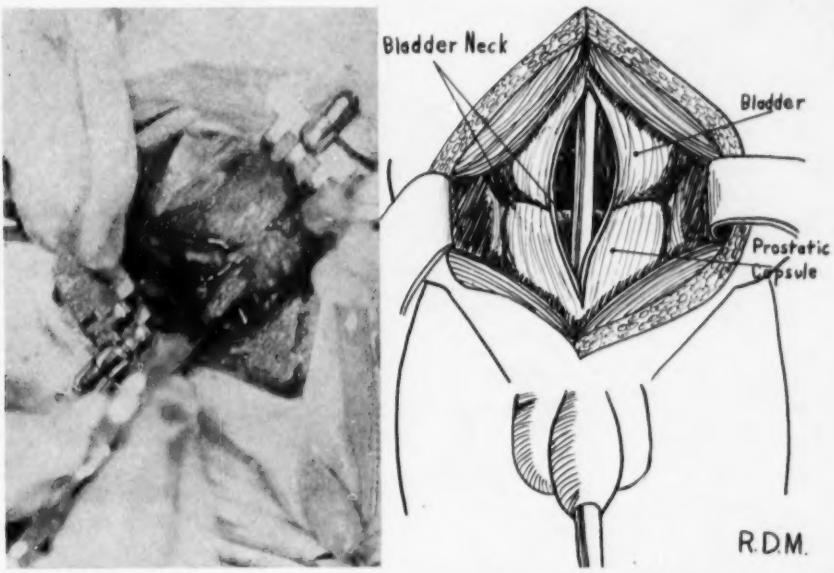

Fig. 1.—Longitudinal incision in the prostatic capsule in a 1-year-old infant, showing a sound in the urethra.

Our technique differed very little from that of the authors previously cited. We found that the passage of a sound before incising the prostatic capsule facilitated location of the urethra. The longitudinal incision in the prostatic capsule was made over this sound (Fig. 1). Owing to the excellent exposure of the vesical outlet, we were able to remove a complete rim of bladder neck tissue instead of the conventional wedge-shaped portion resected from the posterior lip of the bladder neck in the suprapubic approach. In one case this measured as much as 1.5 by 1.0 by 0.7 cm. Light fulgeration with the electrocautery or suturing of the urethral mucosa to that of the bladder were abandoned when a short period of simple digital pressure on the resected area with a piece of oxidized cellulose was found to give adequate hemostasis. It was a relatively simple matter to perform a cystotomy when in one case the metal sound was found to be in a false passage between the bladder and rectum. The full potentialities of extending the longitudinal capsular incision for

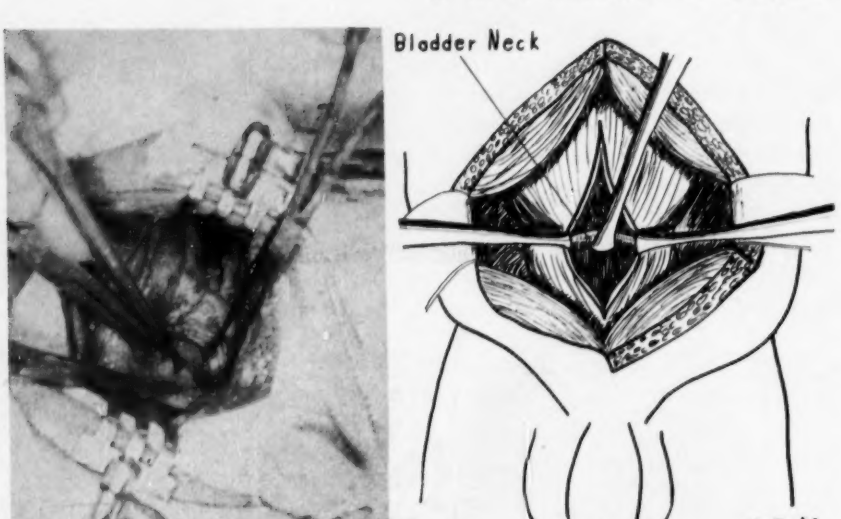

Fig. 2.—Bladder neck is grasped by a clamp and pulled up into the incision prior to resection (same patient as in Figure 1).

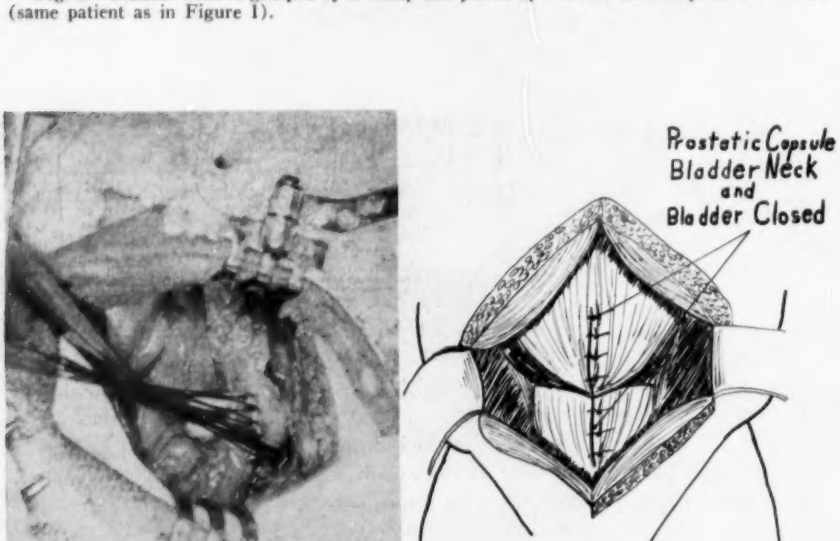

Fig. 3.—Closure of the longitudinal incision in the prostatic capsule and bladder (same patient as in Figure 1).

correcting intra-vesical pathology were not appreciated at first. Therefore, no attempt was made to treat the large diverticulum present in one of our earliest cases. The diverticulum present in a subsequent case was corrected readily by digital dilatation of the orifice to four times its original size. Diverticulectomy, which would have been easy to perform through the retropubic approach, was deemed inadvisable because of its close proximity to a ureteral orifice.

RESULTS

Despite the age of our 1-year-old patient, cystoscopy was accomplished with ease. The surgery was the easiest technically and the postoperative course the most uneventful. The catheter was removed on the fourth, the sutures on the seventh, and the patient was discharged on the tenth postoperative day.

We were particularly impressed by the ease of the operation and the relatively short operating time (45 to 80 minutes). Exposure of the entire prostatic urethra, vesical neck, and, when indicated, the interior of the bladder was excellent. The postoperative course was generally uncomplicated. Temperatures were usually low grade and never remained elevated more than a few days. Hemostasis, during or after operation, was never a problem. Only in one case did hematuria persist as long as five days, while in the remainder, the urine was clear within 48 hours. One of these had grossly clear urine 10 hours postoperative.

In all but one of our patients, water-tight closure with primary wound healing was secured. The urethral catheters were removed on the fourth or fifth day, the child with the false passage being the only one needing a suprapubic cystotomy.

We were able to discharge four patients in our series on the 8th to 14th day. This compares favorably with Burns's 20 patients who were discharged in 8 to 17 days. Hospitalizations of four and eight weeks were necessary in two cases owing to (1) slow healing of a suprapubic cystotomy sinus and (2) an effort to encourage resolution of a large bladder diverticulum by prolonged catheter drainage.

We consider the immediate results in five of our six cases to be excellent. In the remaining case the result can be considered good despite occasional symptoms and the persistence of a large diverticulum which was not treated at the time of operation. Although it now empties almost completely, diverticulectomy may have to be performed if symptoms progress. The diverticulum, which was treated at the time of operation, shows a decrease to almost half its preoperative size. All other children are free of symptoms and their urinary residuals are invariably less than 10 cc.

Cystoscopies were done at intervals of 3, 6, and 12 months. In every case the bladder outlet appeared adequate, and the floor of the urethra was almost level with the trigone. In one it would be difficult to detect evidence of previous surgery on the bladder neck.

We do not consider our follow-up of 6 to 14 months long enough for any final conclusions. The patients have been seen and their urinary residuals checked at monthly intervals for the first year. We shall continue to follow them at six-month intervals for many years.

Pathologically, the specimens were typical, showing either submucous fibrosis, muscular hypertrophy, or a combination of the two.

SUMMARY

Congenital contractures of the bladder neck in six children were successfully resected retropubically, utilizing a longitudinal incision in the prostatic capsule.

This technique offers the advantages of easy access to the prostatic urethra, bladder neck, and interior of the bladder; adequate hemostasis; low morbidity, and, consequently, a short hospitalization.

Dr. Lee Binder gave technical assistance.

REFERENCES

1. Campbell, M.: Clinical Pediatric Urology: With Section on Nephritis and Allied Diseases in Infancy and Childhood, Philadelphia, W. B. Saunders Company, 1951.

2. Campbell, M.: Obstruction of the Lower Portion of the Urinary Tract in Infants and Children, J. Internat. Coll. Surgeons **14**:294-298 (Sept.) 1950.

3. Burns, E.: An Evaluation of the Retropubic Prostatic Operation, J. Urol. **64**:367-372 (Aug.) 1950; Technique of Retropubic Prostatectomy, J. Urol. **65**:856-872 (May) 1951. Burns, E., and Harvard, B. M.: Common Congenital Lesions of the Urinary Tract, J. A. M. A. **146**:419-423 (June 2) 1951. Burns, E.: The Modified Retropubic Operation for Bladder Neck Obstruction in Children, Urological Survey **2**:1 (Feb.) 1952.

4. Lich, R., and Maurer, J. E.: Surgical Relief of Vesical Neck Obstruction in Children, South. Surgeon **16**:127-131 (Feb.) 1950.

5. Hand, J. R., and Sullivan, A. W.: Retropubic Prostatectomy: Analysis of 100 Cases, J. A. M. A. **145**:1313-1321 (April 28) 1951.

WHOLE BODY IRRADIATION ON THE HEALING OF FRESH FRACTURES

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WITH THE addition of the atom bomb to the armamentarium of modern warfare, large numbers of persons may be subjected not only to trauma but also to the effects of whole body x-irradiation. With the exception of experimental work reported in the literature on the effects of local x-rays on fracture healing, we have been unable to find any reports on the effect of whole body exposure to x-rays on the healing of fractures. The purpose of this paper is to report our observations of the effect of whole body x-irradiation on fracture healing in the rat.

MATERIALS AND METHODS

All of the animals used were albino rats of the Wistar strain, weighing over 150 gm. A dose of 500 r will kill 50% of rats of this strain. They are known to require five to six months' growth to reach maturity, with a 300 gm. maximum weight. The rats employed in this experiment were about 3 months of age at the time the experiment began.

A total of 315 rats were employed, 50 of which were utilized as controls. The remaining 257 were exposed to whole body irradiation ranging from 300 to 900 r (the controls were not irradiated). Under ether anesthesia all the rats received a manual fracture of the left femur and were then divided into two main groups: Group 1 received internal fixation of their fractures; Group 2 had no fixation.

In Group 1 there were 166 rats used, of which 35 were controls. The remaining 131 were divided into subgroups subjected to varying amounts of whole body x-radiation, as shown in Table 1. Immediately after irradiation was complete, a small Kirschner wire was inserted intramedullarly into the left femur through the femoral condyles with the knee flexed 90 degrees. The femur was then manually fractured over the edge of a metal tray. The ears of each rat were numbered and the weight of each rat recorded. All rats were housed in metal cages in groups of not over 25 animals and fed the same diet.

At weekly intervals each animal was anesthestized with ether, the weight recorded, and a roentgenogram made of the fractured femur. At these weekly intervals one animal from each subgroup and a control were killed and autopsied. The fracture site was examined for amount of callus and firmness of union and a microscopic section made of the fracture site.

In Group 2 there were 149 rats, 23 of which were used as controls. This group was treated the same as Group 1 except that no fixation of the fracture was employed.

Read before the Section on Orthopedic Surgery at the 102nd Annual Session of the American Medical Association, New York, June 2, 1953.

TABLE 1.— *Group 1 Rats with Fractured Femur and Intramedullary Fixation*

Rats, No.		Radiation Dose, r
35	(controls)	None
25		300
25		400
24		500
25		600
20		700
12		900
Total 166		

TABLE 2.—*Group 2 Rats With Fractured Femur Without Fixation*

Rats, No.		Radiation Dose, r
23	(controls)	None
24		300
24		400
25		500
25		600
28		700
Total 149		

TABLE 3.—*Mortality Experience of Group 1 Rats with Fractured Femur and Intramedullary Fixation*

	Rats, No.	Radiation Dose, r	1st Wk.	2d Wk.	3rd Wk.	4th Wk.	Deaths, No.
Controls							
Subgroups							
	35	None	0	0	1	0	1
	25	300	0	1	0	0	1
	25	400	0	1	4	0	5
	24	500	5 *	4	2	0	11
	25	600	15 †	8	1	0	24
	20	700	9	7	0	0	16
	12	900	7	5	0	0	12
Totals	166	...	36	26	8	0	70

* One anesthetic death.
† Two anesthetic deaths.

TABLE 4.—*Mortality Experience of Group 2 Rats With Fractured Femur Without Fixation*

	Rats, No.	Radiation Dose, r	1st Wk.	2d Wk.	3rd Wk.	4th Wk.	5th Wk.	6th Wk.	7th Wk.	Deaths, No.
Controls										
	23	None	0	0	2	0	0	2	0	4
Subgroups										
	24	300	0	0	0	2	1	0	0	3
	24	400	3 †	1 *	0	0	0	0	0	4
	25	500	5 *	6 *	9 *	1	0	0	0	21
	25	600	2	12	7	4	0	0	0	25
	28	700	3	23	1	0	0	0	0	27
Totals	149	...	13	42	19	7	1	2	0	84

* One anesthetic death.
† Three anesthetic deaths.

OBSERVATIONS

All of the animals were observed for general appearance, water intake, weight loss, use of the fractured extremity, and evidence of clinical union at the fracture site. It was noted that the irradiated rats gave a general unkempt appearance, in that they did not maintain body cleanliness as well as the controls. There was an irregular loss of hair, the remaining hair was dull, and they exhibted moderate to marked loss of vitality and vigor. Their water intake was greatly increased.

The controls of each group had a continuous gain in weight, as did those receiving 300 and 400 r of radiation. Those rats receiving 500 r had a gradual weight loss. Those receiving 600, 700, and 900 r had a marked weight loss. The experience was parallel in both groups.

During the course of the experiment there were 10 deaths attributable to anesthesia (all of these animals were irradiated). Three deaths occurred at the time of surgery; seven occurred shortly after irradiation and during the course of the follow-up. It is to be noted that these deaths occurred in rats receiving 400, 500, and 600 r, which may have been a factor because of reduced vitality.

The mortality of the remaining rats increased proportionately with the dose of radiation. The mortality rate rose rapidly in those receiving 500 r, with the greatest number of deaths occurring by the second or third weeks. In those rats receiving doses of 600, 700, and 900 r, all died except one receiving 600 r and one receiving 700 r in Group 1. Of those receiving the higher doses of x-radiation, the majority died by the end of the second week.

It was noted that those rats who had internal fixation of their fractured femora bore weight on their fractured extremities during the first week and walked normally thereafter. The fractured femora which were not fixed internally were noted to angulate and exhibited gross impairment of function.

Examination of the fractures of the controls in Group 1 revealed that they were springy with small callus at the end of three weeks and firm at the end of four weeks. No marked difference was noted grossly in the healing of the fractured femora of the irradiated rats over the controls. In Group 2 the fractured femora in the controls remained ununited grossly even after seven weeks. A large bulbous fibrous callus could be palpated. No marked difference in the healing of the fractured femora was noted in the irradiated groups over that in the controls of this series. These clinical findings were substantiated for the two groups at autopsy and at gross examination of the fractured femora.

X-Ray Appearance.—Roentgenograms were made of all fractures at weekly intervals and of each specimen. They demonstrated progressive union of the fractures in the Group 1 animals, with no great differences between the controls and the irradiated rats at the end of four weeks (Figs. 1 and 2).

The fractures in the Group 2 animals revealed angulation at the fracture site and massive callus with delayed calcification even at seven weeks (Fig. 3).

Microscopic Examination.—In the 72-hour specimens from the control animals the fracture site revealed a large accumulation of red blood cells in a pink fibrinous network. There were a few small round blue-staining cells which appeared to be young fibroblasts. The hematoma extended beneath the elevated periosteum proxi-

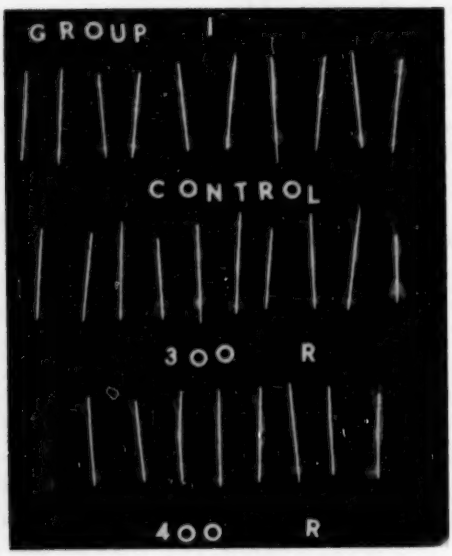

Fig. 1.—X-rays of autopsied rat femora at end of four weeks, showing controls and those receiving 300 and 400r of whole body radiation.

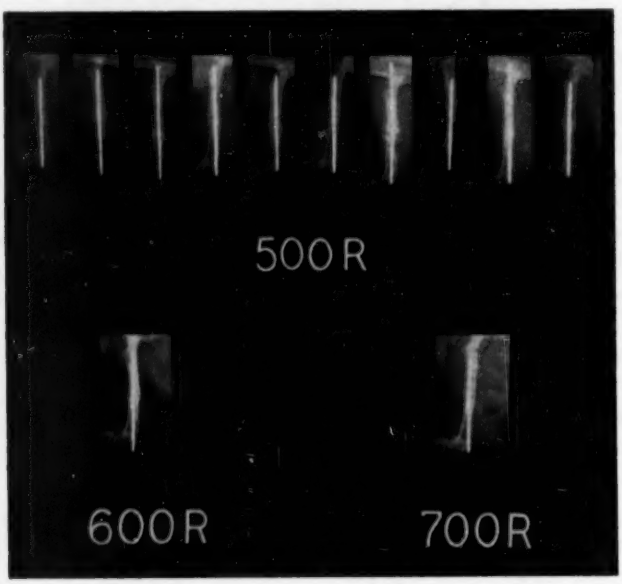

Fig. 2.—X-rays of living rat femora at end of four weeks, showing those that received 500, 600, and 700r of whole body radiation.

mally and distally and filled the medullary canal. Examination of the fractures of the irradiated rats demonstrated no discernible difference at this stage in healing (Fig. 4).

At one week the specimens of the fracture site from the control animals revealed a replacement of the red blood cells by oval and elongated dark-staining cells, probably fibroblasts in a fibrous stroma. In some areas there was beginning proliferation of blue-staining hyaline cartilage cells. In the anchoring and limiting callus there also was seen early pink-staining osteoid. Numerous small blood vessels were present. Examination of the fractures of the irradiated rats demonstrated a retardation of the maturation rate in general. Cartilage cells were less numerous, smaller, and more irregular, and they appeared in small nests in no orderly fashion. With

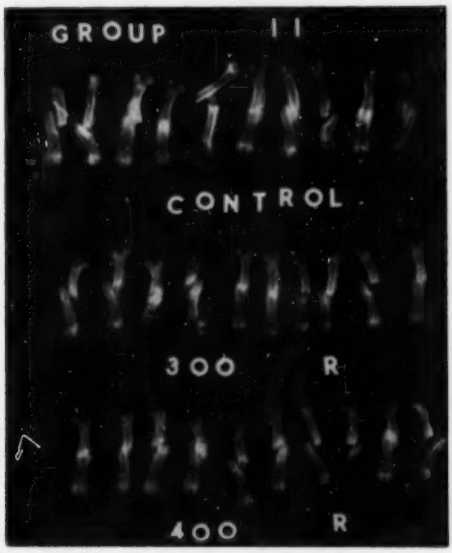

Fig. 3.—X-rays of autopsied rat femora with no fixation at end of seven weeks and those receiving 300 and 400r of whole body radiation.

an increase in the dose of x-radiation, it appeared that the fibrous stroma was more profuse, that the cells were smaller, and that less osteoid appeared. These changes from the normal seemed to parallel directly the dose of radiation received (Fig. 5).

The specimens of the second- and third-week fractures from the control animals revealed a continuation of an orderly maturation of cartilage cells, which was maximum at the two-week period. There was normal-appearing osteoid which was becoming ossified. The bridging and the uniting fibrous callus became completely replaced with calcifying osteoid at the end of the third week. Examination of the irradiated animals revealed irregular development of the cartilaginous nests, retardation of maturation of the cells, and persistence of fibrous tissue in the areas of the bridging and uniting callus. There was formation of osteoid but this seemed confined to the area of the anchoring callus. The osteoid appeared coarser, and the osteoblasts lining these trabeculae appeared smaller, irregular, and fewer in number. All

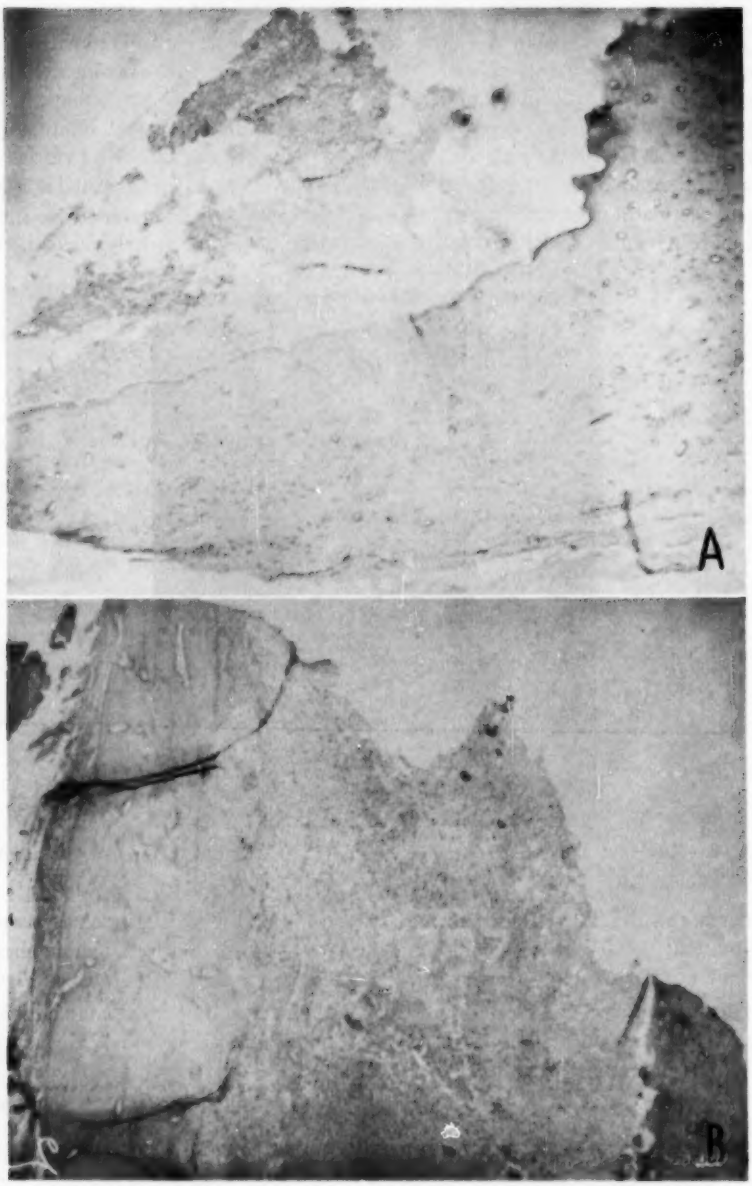

Fig. 4.—Photomicrographs (× 40) showing healing of fractured femur at end of 72 hours: *A*, in control rat; *B*, in rat receiving 900r of whole body radiation.

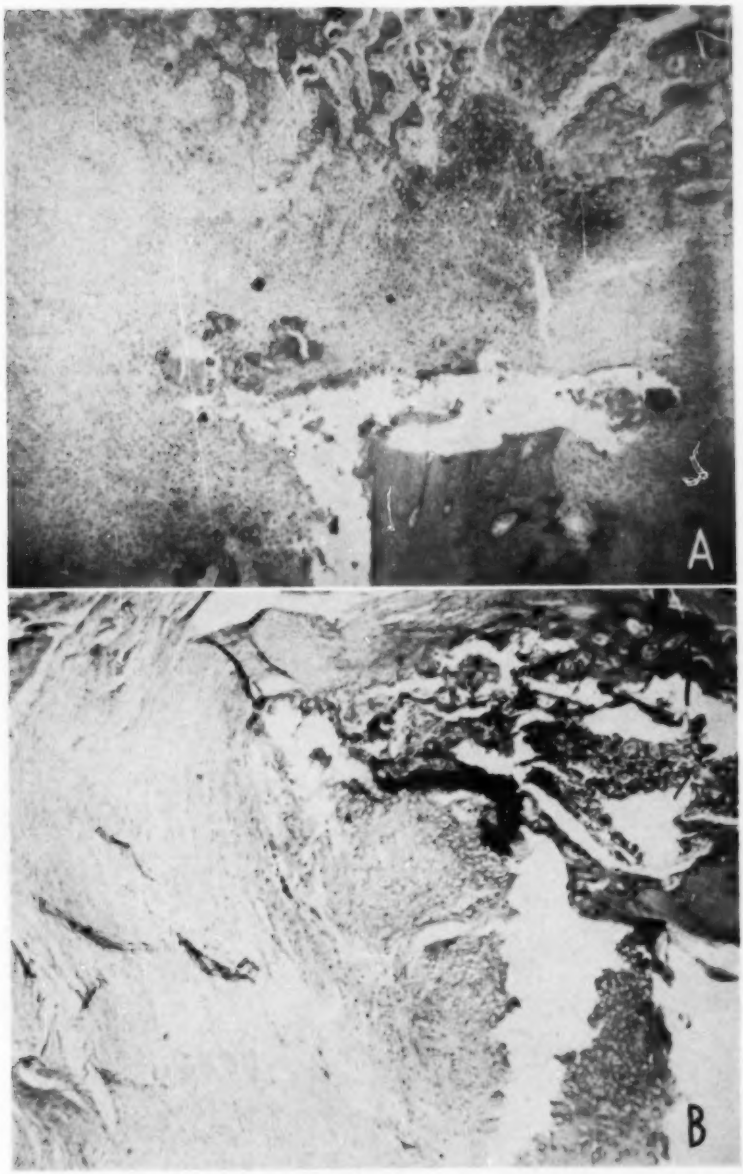

Fig. 5.—Photomicrographs (× 40) showing healing of fractured femur at end of one week: *A*, in rat receiving 300r of whole body radiation; *B*, in rat receiving 700r of whole body radiation.

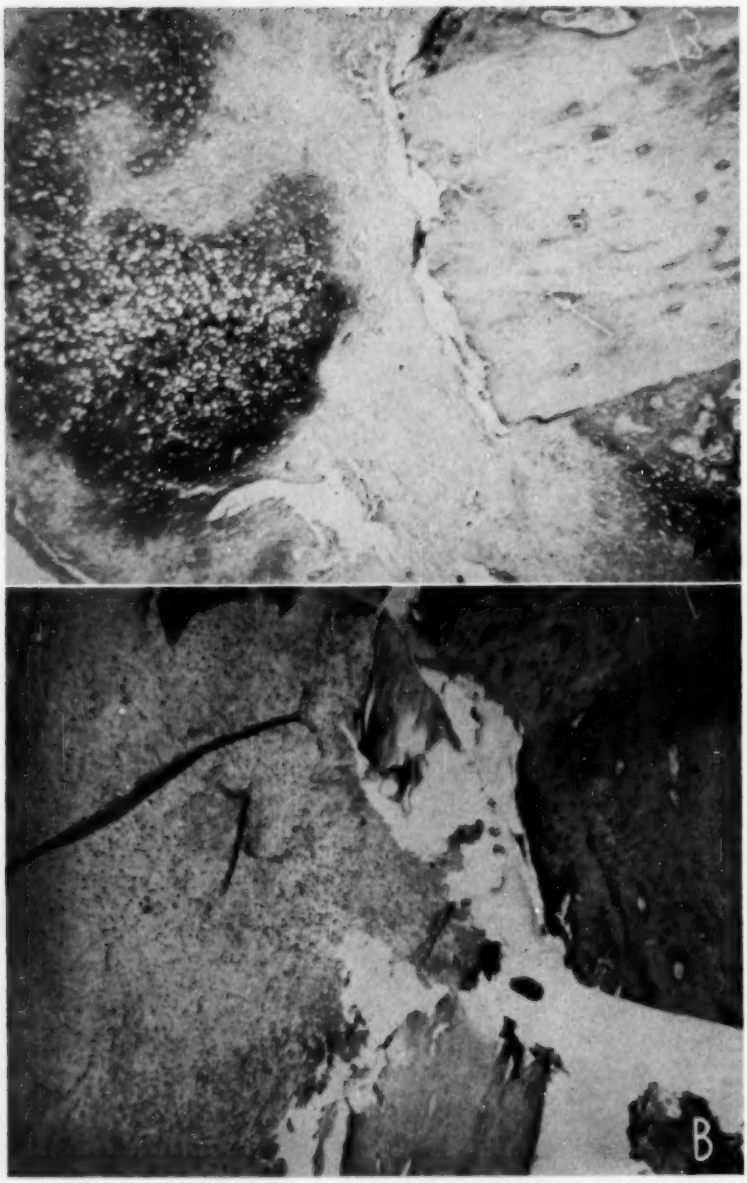

Fig. 6.—Photomicrographs (× 40) showing healing of fractured femur at end of two weeks: *A*, in rat receiving 500r of whole body radiation; *B*, in rat receiving 900r of whole body radiation.

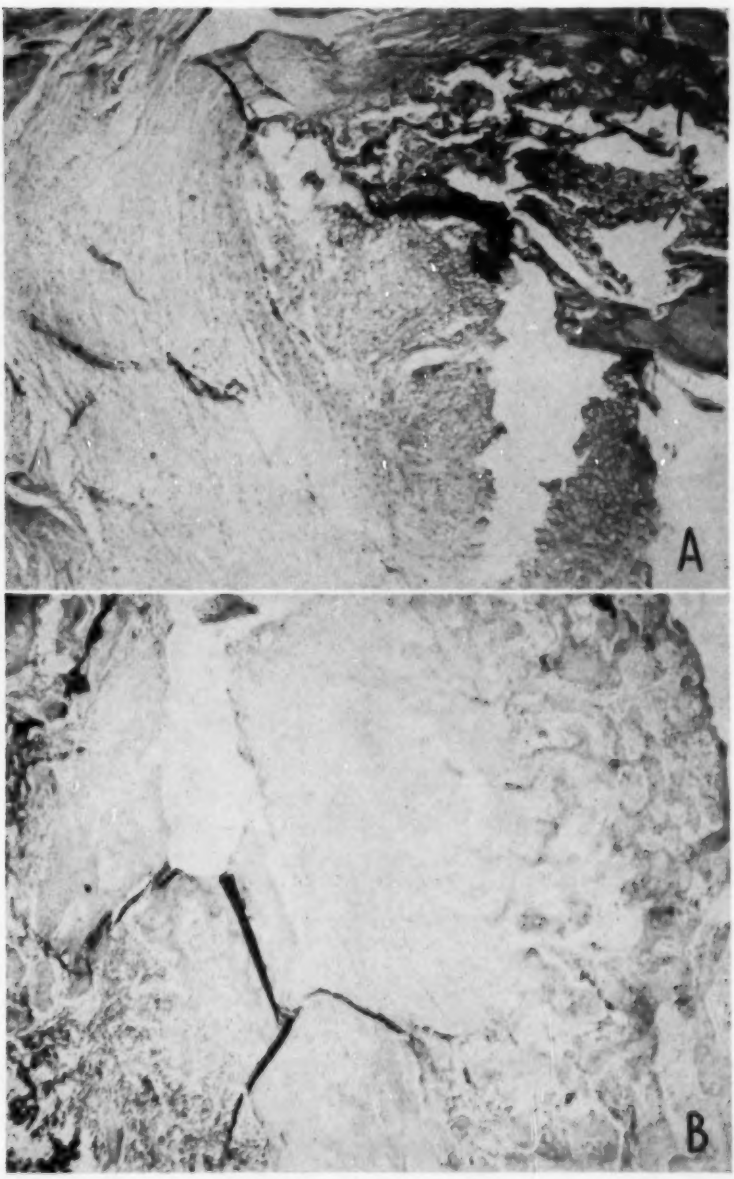

Fig. 7.—Photomicrographs (× 40) showing healing of fractured femur at end of three weeks: *A*, in rat receiving 500r of whole body radiation; *B*, in rat reeciving 700r of whole body radiation.

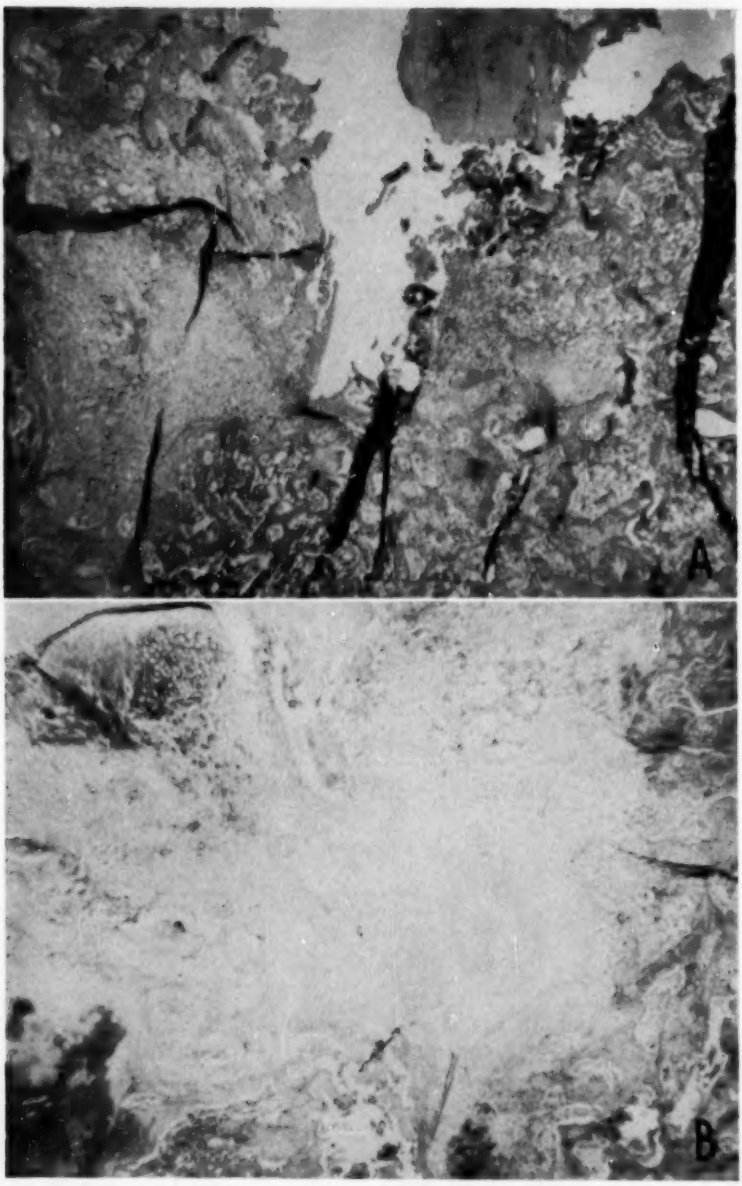

Fig. 8.—Photomicrographs (× 40) showing healing of fractured femur at end of four weeks: *A*, in rat receiving 500r of whole body radiation; *B*, in rat reeciving 700r whole body radiation.

seemed to have poorer staining characteristics than the controls. Again these changes were noted to be directly proportionate to the dose of radiation received (Figs. 6 and 7).

At the fourth and fifth weeks examination of the specimens of the fracture of the control animals revealed complete replacement of the osteoid and cartilage cells, with good mature trabeculations lined with normal-appearing osteoblasts. Examination of the fractures of the irradiated animals again revealed further maturation of the irregular-appearing nests of cartilage cells. Osteoid material appeared further advanced in its development, but these changes again were noted to occur in the area of the anchoring and limiting callus. Persistence of fibrous material in the area of the uniting callus again was seen. These changes, too, were noted to parallel the dose of radiation received (Fig. 8).

The microscopic examinations of the specimens of the fracture site in the control animals in the Group 2 rats revealed a large fibrous callus. A few cartilage cells made their appearance after three weeks, with a small amount of osteoid being deposited. After five weeks the osteoid was being calcified, which seemed to be confined to the zone of the anchoring callus. At seven weeks this calcified osteoid was more profuse but still confined to the region of the anchoring callus. The bridging and uniting callus remained fibrous without healing of the fracture. The delay in maturation of the callus in the irradiated group of rats was again noted to be proportionate to the dose of x-rays received as observed in the Group 1 rats.

COMMENT

Extensive whole body irradiation of the experimental animals caused marked weight loss, debility, and mortality, which were proportionate to the dose of radiation received. The greatest mortality took place during the first and second weeks. Only two animals receiving the usual fatal dose of x-ray survived.

Microscopically it was demonstrated that extensive irradiation resulted in a delay in the healing of the fracture which was greatest during the first three weeks. The two animals surviving the usual fatal dose of x-rays began to gain weight after the fourth week. Microscopically, more calcifying osteoid began to develop in the fracture site. Although the development was retarded and irregular, it was progressive. These findings are in agreement with those of Regen and Wilkins,[1] who found that the depression of the phosphatase level was greatest during the second and third weeks in animals whose fractured bones were locally irradiated and that healing was delayed during this period. These findings are at variance with those of Brooks and Hillstrom,[2] who failed to find any perceptible difference on bone regeneration following local x-rays.

If rats survive the effects of the trauma of fracture and whole body irradiation, healing of the fracture will be delayed but can be expected to progress to complete healing after the effects of irradiation have been overcome.

SUMMARY AND CONCLUSIONS

Whole body x-irradiation of young adult white rats alters the normal maturation and orderly development of cartilage and ossifying osteoid, the result being a delay in the healing of the fracture.

ABSTRACT OF DISCUSSION

DR. A. R. SANDS, JR., Wilmington, Del.: Col. Spittler and his group are to be congratulated on working on a subject which may one day be of tremendous clinical importance to all of us, but which day all of us hope will never arrive. There has been little or no real study on the healing of fractures in associations with body x-irradiation. These experiments of the authors on 315 rats represent an enormous amount of work by many persons and are certainly original.

The authors have proved convincingly that the exposure of rats to 500 r or more will result in an almost 100% mortality rate. They also have definitely proved that fixation of the fracture is a necessity for healing in seven weeks or less. The experiments would have been more complete if the reports had included observations of more than seven weeks on the Group 2 rats. It is quite likely that many of the fractures in the Group 2 rats would have united after this time. If the authors had made weekly correlations of the amount of callous, firmness of union, and microscopic sections of autopsied rats, the study would be of more significance. I trust this information will be given in the final paper.

The question arises concerning whether these rats were adolescent and not adult, since the authors state Wistar strain rats "require five to six months to reach maturity." If adolescent, bone formation should be more rapid.

I do not believe that the work on this subject by Regen and Wilkins, reported in 1936 and referred to by the authors, is comparable to this study. Regen and Wilkin's work was entirely on the effect of local irradiation on fracture healing and phosphatase production. Also, in the work of Regen and Wilkins, rabbits were used, and these animals are notably unsatisfactory for the study of bone formation because of their ability to produce bone rapidly with the least provocation.

REFERENCES

1. Regen, E. M., and Wilkins, W. E.: The Effect of Large Doses of X-Rays on the Growth of Young Bone, J. Bone & Joint Surg. **18**:61, 1936; The Influence of Roentgen Irradiation on the Rate of Healing of Fractures and the Phosphatase Activity of the Callus of Adult Bone, J. Bone & Joint Surg. **18**:169, 1936.

2. Brooks, B., and Hillstrom, H. F.: Effect of Roentgen Rays on Bone Growth and Bone Regeneration: Experimental Study, Am. J. Surg. **20**:599, 1933.

Case Reports

CHLORIDORRHEA

Syndrome Associated with Diarrhea and Potassium Deficiency

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NEW YORK

THE ASSOCIATION of potassium deficiency with diarrhea is rather common, the potassium deficiency being secondary to the diarrhea.

Usually diarrhea is associated with acidosis because of the excess of base over anions in large bowel excretions. The patient who forms the basis of this report presented the paradoxical picture of severe diarrhea associated with alkalosis. The unusual status of an excess of chloride over base in the diarrheal stool of this patient with an associated hypokalemic alkalosis and severe clinical sequelae has many features in common with the unusual instances of infants with congenital alkalosis and diarrhea presented by Gamble and his associates [17] and Darrow.[10] This report describes the results of studies performed upon the patient and the effects of different therapeutic modalities upon the entity. The chemical methods employed have been reported.* Stool electrolytes were determined by the method of Wallace.

REPORT OF A CASE

A 66-year-old white man was admitted to the hospital on May 30, 1949, because of large bowel obstruction. His symptoms dated back to one year before when slight melena with sporadic bouts of diarrhea developed. In the periods when he had no diarrhea he was asymptomatic. Two weeks before admission diarrhea of a marked degree developed followed by painless abdominal distention of six days' duration. He passed neither feces nor flatus for the two preadmission days. His past history was noncontributory.

Physical examination revealed a chronically ill-appearing white man with a moderately distended abdomen which had a tympanitic sound on percussion. The patient was alert, clear of mind, and cooperative. The remainder of the physical examination was essentially negative except for evidence of hypertrophic arthritis involving the joints of both hands. His temperature was 99 F., pulse rate 60 beats per minute, respirations 20 per minute, and blood pressure was 170 mm. Hg. systolic and 104 mm. diastolic. The laboratory findings on admission were not remarkable. The blood hemoglobin was 15 gm. per 100 cc. Serum chloride was 93 mEq. per liter and the carbon-dioxide-combining power slightly elevated to 29 mEq. per liter. The blood urea nitrogen was elevated to 23 mg. per 100 cc. The patient was treated by a long intestinal tube attached to Wangensteen suction, and he was maintained on parenteral fluid administration, which consisted of an average of 1,500 ml. of dextrose and 0.9% saline solution (no potassium was given). Four days after admission a transverse colostomy was performed with the use of gas-oxygen-ether anesthesia and was well tolerated. During the six-day period that intestinal intubation and suction were applied, 6,750 ml. of fluid was aspirated. The aspirated fluid con-

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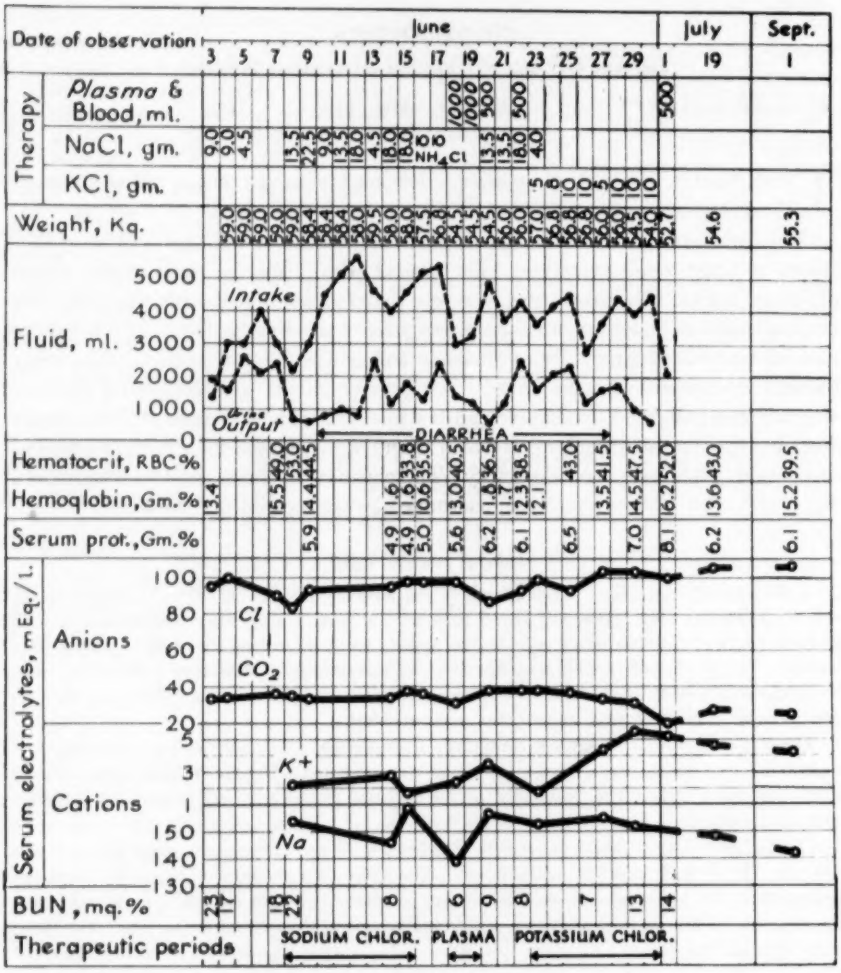
*References 1 and 2.

tained the following quantities of electrolytes: chloride, 470 mEq.; sodium, 302 mEq., and potassium, 200 mEq. The colostomy drainage was of moderate quantity for the first four days after the stoma was opened, but it gradually increased in quantity and by the eighth post-colostomy day as much as 3 liters of foul, foaming, diarrheal stools were expelled per day.



Ordinary constipating agents had no effects upon the diarrhea. The patient who had been lethargic and quietly disinterested in his environment suddenly experienced hallucinations and made violent attempts to jump out of bed, necessitating restraints. He became markedly confused and disoriented. Analysis of his serum at this time revealed a hypochloremia of 83 mEq. per liter; carbon-dioxide-combining power, 35 mEq. per liter, and serum potassium, 2.2 mEq. per liter (Chart).

The treatment of the hypochloremic hypokalemic alkalosis was divided into five therapeutic periods, which are summarized in the Chart. An attempt was made to give one repair solution

during each of these periods to note the effects of each upon the clinical symptoms and the metabolic balance of the patient.

Metabolic Alterations During Different Treatment Periods.—Treatment Period 1 (Eight Days): Sodium Chloride Administration. During the first therapeutic period (eight days) sodium chloride solutions, as 0.9% sodium chloride and 5% dextrose solution, were given intravenously. During the first two days on this regimen, after 36 gm. of sodium chloride had been administered, complete improvement in his mental status became evident. He became oriented, cooperative, and somewhat jovial. He had a vague memory of the preceding days of disorientation. Although he was mentally alert, he complained of generalized weakness and easy fatigability after the mildest exertion, and he manifested a stubborn reluctance to ambulate. He was given a regular diet, which he ate (unfortunately measurements of the constituents of his food intake were not made), and was given, in addition, a continued regimen of intravenous sodium chloride therapy (averaging 14.6 gm. of sodium chloride daily intravenously and an unmeasured portion of salt in his diet). He had no distaste for oral salt.

Severe diarrhea persisted throughout the entire period of sodium chloride administration. A remarkable finding was the large quantities of chloride being excreted in the stool (chloridorrhea). At the commencement of this study (June 5) 800 ml. of stool were measured and the chloride content of 28 mEq. more than doubled the sodium content of the feces (12 mEq). This

TABLE 1.—*Stool Content per Twenty-Four Hours*

	Start of Study, 6/5	During Sodium Chloride Administration, 6/11	End of Sodium Chloride Administration, 6/15	After Ammonium Chloride Administration, 6/17	After Plasma Administration, 6/20	After Sodium Chloride Administration, 6/23	After Potassium Chloride Administration, 6/29
Stool, ml.	800	3,000	2,800	3,400	2,800	1,500	300
Chloride, mEq.	28	87	122	147	89	96	17
Sodium, mEq.	12	40	70	52	40	51	12
Potassium, mEq.	18	23	44	28	20	24	8
Fat, gm.	..	..	10	..	8	..	3
Nitrogen, gm.	..	..	2.2	..	1.8	..	0.9

excess of chloride over sodium is a most unusual finding. The liquid feces increased in amount as the sodium chloride administration continued and equalled 3,000 ml. on June 11 in the midst of the sodium chloride therapeutic regimen, and 2,800 ml. on June 15 at the completion of this regimen. The large quantities of chloride excreted in the stool are presented in Table 1, and in each instance the chloride content far exceeds the sodium content. In fact the chloride content exceeded the total cation (Na and K) of the stools. No other stool cations were determined and therefore it is not known to which positive radical the excess chloride was bound. A continued presence of potassium within the stools persisted despite a low plasma level. Stools were measured for the total quantity and content of electrolytes during specific 24-hour periods. It was not possible to perform measurements throughout the entire period of study because of difficulties of collecting the liquid feces pouring through the colostomy.

The urinary content of electrolytes is presented in Table 2, which reveals a continued excretion of chloride in the urine but in far less quantities than in the stool and always much less than the sodium content of the urine. Urinary potassium in significant quantities was always present.

Volume studies are presented in Table 3 and reveal but a very slight increase in plasma volume (200 ml.). It is difficult to account for the decrease in hematocrit and hemoglobin on the basis of this small increment in plasma volume (as measured by the Evans blue dye technique). It thus seems possible that some unexplained loss of red blood cells has occurred. A large increment of the interstitial space (thiocyanate space minus plasma volume) of 2.2 liters is noted during this therapeutic regimen.

TABLE 2.—*Electrolyte Content of Urine, MEq. per Twenty-Four Hours*

	Sodium Chloride													Ammonium Chloride		Plasma		Sodium Chloride				Potassium Chloride						
	6/3	6/4	6/5	6/6	6/7	6/8	6/9	6/10	6/11	6/12	6/13	6/14	6/15	6/16	6/17	6/18	6/19	6/20	6/21	6/22	6/23	6/24	6/25	6/26	6/27	6/28	6/29	7/19
Chloride, mEq.	..	..	21	39	0	7	22	69	62	..	..	39	38	30	34	..	35	39	..	234	..	174	124	206	150	137	68	40
Sodium, mEq.	..	..	20	51	28	46	68	87	90	..	..	77	74	11	9	..	56	48	..	250	..	181	140	227	165	153	75	50
Potassium, mEq.	..	..	45	60	34	56	40	73	51	..	..	59	56	44	32	..	40	37	..	55	..	36	19	27	22	20	15	12
Nitrogen, gm.	..	..	4.0	..	..	5.6	..	..	4.2	..	..	..	6.2	..	..	..	..	4.5	..	2.3	..	5.5	..	..	..	..	4.0	..

Analyses of a muscle biopsy (deltoid) from this patient after the sodium chloride regimen is presented in Table 3. The techniques of analysis are those described by Darrow.[9] The water content of 22.4 mEq. is somewhat diminished. The nature of the severity of the disturbance is demonstrated by the extremely low value for the potassium content and the extraordinary high sodium level. If the potassium content of the muscle is expressed in mEq. per 100 gm. of fat-free solids, the very low level of 26 mEq. of potassium reveals the severity of the potassium deficiency (normal level is approximately 45 mEq). It thus becomes apparent that large quantities of sodium have replaced intracellular potassium.

Treatment Period 2 (Two Days): Ammonium Chloride Administration. The plasma alterations resulting from the intravenous administration of 20 gm. of ammonium chloride (Chart) consisted in a slight but transient decrease of the carbon-dioxide-combining power and a sharp drop of the serum sodium from its high level of 160 to 138 mEq. per liter. Analysis of the stool after administration of ammonium chloride reveals the largest output measured and the severest chloridorrhea of this study (Table 1). Significant quantities of chloride are excreted in the urine but a marked drop in the urinary sodium content occurs. No volume studies or muscle biopsies were obtained during this therapeutic period.

Treatment Period 3 (Three Days): Plasma Administration. The administration of 2 liters of plasma containing approximately 140 gm. of protein increased the serum protein concentration to a normal level (Chart), produced a significant decrease in the plasma chloride level from 100 to 83 mEq. per liter, had no effect upon the carbon-dioxide-combining power, increased

TABLE 3.—*Volume Studies*

Date	6/5	6/15	6/20	6/29
Plasma volume, liters	2,400	2,000	3,350	2,980
Interstitial space, liters	8,000	10,250	9,700	9,000
Weight, kg	50	58	56	54.5

the potassium level from 2.1 to 3.3 mEq. per liter (presumably the effect of the potassium within the administered plasma), and produced a sharp decrease in the serum sodium. Each of these changes was transient. In a previous study Ariel, Abels, Pack, and Rhoads [3] demonstrated a correction of hypochloremic alkalosis by the administration of plasma. The failure to accomplish any significant change of the carbon-dioxide-combining power in the patient by plasma administration reveals that a different defect existed here from that which could be corrected by plasma administration. The analysis of the stool after plasma administration (Table 2) revealed some diminution of the electrolyte content of the unrelenting diarrhea. No significant change in the urinary profile of electrolytes was noted. Volume studies revealed a 700 ml. increment in the plasma (which might account for the decrease in the plasma concentration of the chloride and sodium which occurred). A decrease in the interstitial space of 500 ml. occurred. During this same period a loss of 2 kg. of body weight occurred. If the administered fluid had been dissipated in the diarrheal stools, the effects of the plasma could be interpreted to have effected a translocation of fluid from the interstitial spaces into the circulation (presumably a result of increased oncotic pressure exerted by the plasma protein). A muscle biopsy was not obtained for this period.

Because of anemia the patient was given two 500 ml. whole blood transfusions subsequent to the plasma administration period (Chart). He was also returned to the sodium chloride administration regimen to note if the administered chloride would be handled differently by the body with its replenished plasma volume and protein content. The serum chloride returned to its level of 100 mEq. per liter. A decrease in the quantity of the stool was noted, but no change in its electrolyte content occurred. A tremendous quantity of urinary sodium (250 mEq.) and chloride (234 mEq.) was excreted. The exact explanation is not apparent but is probably due to the diuretic effect of restoring plasma protein concentration. A previous study has indicated that a high level of plasma protein permits retention of administered saline solutions

in the plasma for deliverance to the kidney when indicated rather than having the administered saline diffuse into the interstitial space when hypoproteinemia exists.[1]

Treatment Period (Eight Days): Potassium Administration. The most dramatic changes occurred both in the physical status of the patient and in his metabolic response with the intravenous administration of potassium chloride. Associated with the general feeling of well-being, with improved muscle tone there was a rather abrupt cessation of the watery diarrheal stool. The foul odor decreased in intensity and the improved consistence resulted in semi-formed stools. A progressive decrease in the serum carbon-dioxide-combining power, as well as a sharp increase in the serum potassium from 2 to over 5 mEq. per liter, occurred. The serum sodium remained rather high at 150 mEq. per liter. Stool studies performed after the potassium chloride regimen revealed a total fecal output of 300 ml. Although the chloride content of the feces had decreased to 17 mEq., it still exceeded the 12 mEq. sodium content of the stool. Despite the administration of large doses of potassium, the potassium content of the feces diminished most significantly from previous periods during which no potassium was administered. The urine reflected an exodus of large quantities of sodium and, to a slighter extent, of chloride from the body. The urinary potassium was also less than during the previous periods of potassium deprivation. Beneficial changes were also reflected in volume studies, which revealed a decrease in the interstitial space of 9 liters (Table 3). Analysis of the muscle biopsy (Table 4) revealed a decrease in the total water from the previous level and an increase in the muscle chloride. The most significant changes occurred in the muscle sodium and potas-

TABLE 4.—*Muscle Composition (MEq./Kg. Fat-Free Tissue)*

	During Sodium Chloride Administration, 6/15	After Potassium Chloride Administration, 7/1	Two Months Later, 9/1
H_2O, ml./kg	795	780	786
Chloride, mEq.	22.4	26.6	29.0
Sodium, mEq.	83.5	50.3	33.4
Potassium, mEq.	53.8	78.4	87.0

sium content, the muscle potassium increasing to 78.4 mEq. per kilogram of wet tissue (35.6 mEq. per 100 gm. of fat-free solids). This value is still somewhat lower than the normal level, despite the administration of large quantities of potassium, and indicates the tremendous potassium deficit which had existed in the cells. Associated with the increased tissue potassium was a drop in the tissue sodium to 50.3 mEq. per kilogram of wet tissue (22.8 mEq. per 100 gm. of fat-free solids), which is still an abnormally high value. It cannot be determined from these data whether a more intensive form of potassium treatment would have completely corrected the intracellular defect or whether the element of time is essential.

Two months later the patient presented normal values for his plasma constituents. A muscle biopsy revealed that the potassium had increased to 87 mEq. per kilogram of fat-free tissue (40.6 mEq. per 100 gm. of fat-free solids) and the sodium had descended to 33.4 mEq. per kilogram of fat-free tissue (15.6 mEq. per 100 gm. of fat-free solids).

The patient was discharged on July 2, 1949. When readmitted on July 19, all serum chemical findings were within normal levels (Chart). A resection of the sigmoid colon for diverticulitis was performed, from which the patient made an uneventful convalescence.

He was again admitted on Sept. 1, 1949, for closure of the colostomy, and again all blood studies were normal. He did not present any evidence of diarrhea. Unfortunately, fecal studies were not performed.

COMMENT

One of the unusual phenomena of this case is that the intractable severe diarrhea which resisted ordinary methods of control was apparently aggravated by the intravenous administration of chloride solutions and subsided rapidly after the intra-

venous administration of potassium salts. The other unorthodox finding is the large amounts of chloride in the stool.

Certain features of the metabolic derangements manifested by this patient conform to the orthodox concepts of electrolyte abnormalities. The diarrhea and withdrawal of large quantities of electrolyte-containing solution instituted the defective electrolytic structure consisting of hypochloremia, hypokalemia, and alkalosis. The intravenous administration of large quantities of chloride-containing solutions temporarily corrected the hypochloremia. The persistence of the alkalosis after chloride administration demonstrates that the fundamental defect had not been corrected by the chloride. Volume studies of the plasma and extracellular space and analyses of muscle for its water and electrolyte content permit a suggested explanation of the sequence of events which occurred when large quantities of chloride were intravenously administered to the patient suffering from hypokalemic alkalosis.

The sharp increase in the interstitial volume, during which time a loss of 1 gm. of body weight occurred, indicates the direction of the alterations of fluid distribution and suggests that the extracellular space is flooded with chloride-containing fluid. Decreased body weight in the presence of this extracellular increment suggests a diminution of intracellular water.

Usually in potassium deficiency chloride is not properly reabsorbed from the glomerular filtrate, hence alkalosis develops or persists and is probably an important factor of the bizarre phenomenon observed in our patient. The data show an intracellular diminution of potassium, which, surprisingly enough, continues to be excreted in the urine and feces. Since chloride is being excreted in far greater quantities than sodium, it is suggested that sodium has been deposited intracellularly. It would appear that because of the fundamental intracellular defect (potassium deficiency) the body is attempting to excrete the improperly administered repair solution (sodium chloride). The material is being administered in such quantities as to tax the body's excretory capacities and a reserve of the unwanted solution accumulates in the extracellular compartment, producing an extracellular edema.

The dramatic subsidence of the mental symptoms of confusion, disorientation, and maniacal attempts to thrash out of bed after the administration of sodium chloride solutions indicates that these symptoms were manifestations of sodium chloride and water disturbance. However, the symptoms of generalized muscular weakness, rapid fatigability, and great reluctance to ambulate which this patient presented, even after the mental symptoms had been successfully combatted by sodium chloride and fluids, are no doubt related to potassium deficiency. (Neither paralysis nor convulsions occurred during this investigation.)

The persistence of alkalosis in the presence of potassium deficiency, which resists every effort aimed at its reduction—exclusive of potassium administration, has been adequately described.[7] The administration of potassium salts to this patient rapidly reduced the carbon-dioxide-combining power to a normal level and increased the plasma potassium content.

Potassium deficiency is known to cause hypomotility to the point of atony of the gastrointestinal tract. In the patient under investigation, hypokalemia was associated with a profuse diarrhea. Diarrhea in itself does produce potassium deficiencies. In fact, the brilliant studies by Darrow[8] of the diarrhea in children led

to his recognition of the potassium deficiency with its resultant effect upon the entire metabolic balance of the individual patient. He clearly demonstrated that the replacement of potassium was critical to the recovery of the patient. Diarrhea associated with sprue,[19] lymphosarcoma, abdominal Hodgkin's disease, tuberculous lymphadenitis, and other entities has been described as producing potassium deficiency.† All reported instances of diarrhea reveal the classic entity of fecal excretion of large quantities of sodium, little if any chloride, and variable amounts of potassium. Two exceptions have been reported independently by Darrow [10] and by Gamble and his associates [17] whose patients excreted much chloride in the stools and will be discussed later. The unusual feature of the patient herein presented is also the abnormally large quantities of chloride in his diarrheal stool. Throughout all periods of this study, the chloride content of the stool exceeded its sodium content. The urine also contained significant quantities of chloride but always to a slighter degree than sodium. An explanation for the chloridorrhea is not manifest from these data. Extremely rapid peristalsis could conceivably transport a chloride excess in intestinal juice from the stomach to the rectum. This patient did not reveal any evidence of increased peristalsis. Gastrocolic fistula exists with chloridorrhea, but this situation is metabolically akin to that produced by vomiting. This patient did not have a gastrocolic fistula.

Roentgenograms of the intestinal tract did not reveal any evidence of ectopic gastric mucosa, which conceivably could account for an increased quantity of chloride in the feces. Normally the chloride of the gastric juice is absorbed within the intestine. Whether the presence of a colostomy exerted an affect is not known. It is true that the colonic effluent would not have contact with the mucosa of the distal portion of the transverse colon and the descending colon where the electrolyte content of the stool could be altered. However, it is felt that the presence of the colostomy was not the culprit, for other patients with colostomies, whose fecal electrolytes were analyzed, did not reveal chloridorrhea. Whether or not the diverticulitis had any effect is not known, but it is doubtful, for the disease was localized to the descending colon and chloridorrhea apparently results from activity of the entire small and large intestines.

This patient demonstrates either a defect in the absorption of the chloride with its resultant excretion or an abnormal secretion of chloride from the plasma into the intestinal tract. If the defect be abnormal absorption, it would appear that it is limited to the chloride ion because of the relatively normal values for stool fat and nitrogen throughout all periods of study.

Dennis and Visscher [18] have demonstrated that the absorption of sodium and chloride from the intestine is effected with transfer of water. Since more sodium and chloride are absorbed than water, that remaining in the bowel is hypnotic to plasma. Simultaneously, transport of sodium, chloride, and water occur from the plasma into the intestine. When divalent ions are present (sulfate, aluminum hydroxide, etc.), chloride enters the blood more rapidly, while the transport of water from the intestine is slowed down. These mechanisms are not produced by simple osmotic exchanges but represent energy expended in overcoming the osmotic gradient which is dependent upon cellular activity.

† References 21 and 23.

Because chloridorrhea persisted and was intensified when chloride solutions were intravenously administered, it would suggest that a diffusion of electrolytes occurred from the plasma into the intestinal tract and the error was one of abnormal ingress into the intestine rather than faulty absorption of chloride from the intestinal tract. The exact reason is unknown, but the cure of the diarrhea and the subsidence of the chloridorrhea following the administration of potassium suggest that potassium balance may in some manner be involved in this syndrome.

It is most unusual for chloride to be excreted into the colon because usually the opposite reaction occurs, namely, secretion of excess chloride from the bowel into the plasma. This occurs not infrequently after ureterocolic anastomosis and produces the bothersome clinical syndrome of hyperchloremic acidosis.‡

When chloride solutions are administered to patients suffering from hypokalemic alkalosis, the chloride is rapidly excreted via the kidneys. It is theoretically possible that potassium deficiency alkalosis was responsible for the extrusion by the body of the chloride ion. Why the colonic route for excreting chloride was utilized is not known. If this is the explanation, then it is theoretically conceivable that the diarrhea may have been a mechanism of excreting chloride in solution. The data in this case do not prove this hypothesis but are suggestive and focus attention upon potassium deficiency alkalosis for further investigation.[18] Although potassium administered intravenously produced an abrupt diminution in the diarrhea and total fecal chloride excreted, chloridorrhea persisted, and chloride in excess of sodium continued to be excreted. If the above explanation of the mechanism is correct, it would suggest that the deficit had not been corrected. It is more probable, however, that a more complex situation exists.

Gamble has described an instance of an infant who excreted large quantities of chloride in the stool and almost none in the urine. The patient died, and at autopsy no anatomic explanation for the electrolyte defect could be found. Certain points of similarity exist between Gamble's patient and the patient of this report, namely, the voluminous diarrhea, persistent alkalosis, and the abnormal presence of an excess of chloride over sodium in the stool. Gamble believed that the diarrhea was incidental to some unidentified disturbance of water and electrolyte control which compels removal of chloride exclusively by way of the intestinal tract. He does not believe that there is an ungoverned removal of the chloride via the stool but rather that some force is successfully effecting an excretion of chloride. All efforts to raise the plasma chloride level were resisted, and, when accomplished, it was of short duration. He believes that the maintenance of a low plasma chloride appears to be part of a distortion of the physiochemical system of the body fluids and is not a primary event. Our patient differs from the one reported on by Gamble in that in our patient a high serum chloride exists in the presence of severe alkalosis. This is probably the result of the large doses of sodium chloride administered to our patient by which a normal plasma chloride level was achieved. The persistent severe alkalosis reflects that the fundamental defect was not corrected. The apparent aggravation of the diarrhea by the administration of chloride solutions would serve to support Gamble's hypothesis that the diarrhea is a means whereby the body rids itself of the

‡ References 22 and 23.

unwanted chloride. Our patient also differs from Gamble's in that in our patient appreciable quantities of chloride were excreted by the urine, whereas in Gamble's patient none was excreted by that route.

Darrow reports on a similar patient who had persistent diarrhea from the time of birth until the time Darrow made his report, which was when the child was 2 years and 11 months old. The essential features were diarrhea, chloridorrhea, and hypochloremia. Darrow apparently identified the defect which Gamble had surmised and attributed some of the abnormal findings (hypochloremia, alkalosis, and others) to a deficiency of potassium. The administration of potassium salts by Darrow gave some relief and produced an improvement of some of the metabolic constituents. Darrow's patient manifested an extracellular dehydration and intracellular overhydration.

There are many points of similarity between our patient and the one reported on by Darrow. The severe potassium deficiency in our patient, as evidenced by the low plasma potassium level and the extremely low tissue content, was probably the culprit in producing many of the observed disruptions of electrolyte balance. The administration of copious quantities of saline solutions to our patient accounts for the expanded interstitial space, in contrast with Darrow's patient whose extracellular space was contracted. The alkalosis was maintained despite every effort to correct it in order to maintain the new equilibrium established by the potassium deficiency, a situation so vividly described by Darrow. The bicarbonate ion is usually a subservient ion which rapidly and with great agility either increases or decreases in quantity in answer to the demands of sodium and chloride exchange. Here it maintains a high fixed level which commands the quantity of chloride within the body and exerts a powerful stimulus for the excretion of excess chloride. The sequence of events which occurred after the administration of potassium salts were dramatic. A veritable chain reaction was instituted with ingress of potassium into the cells: extrusion of sodium from the cells, excretion of large amounts of chloride and sodium shortly after potassium was given, decrease in the interstitial space, lowering of the carbon-dioxide-combining power, and increase of the plasma potassium. Associated with the corrected metabolic values, the patient felt stronger and well. There was a rapid diminution of the watery diarrhea. Although the chloride content of the stool decreased markedly, a mild degree of chloridorrhea persisted at the completion of the experiment. (A normal potassium and sodium content of tissues had not been attained at that time, as evidenced by tissue analysis.) This symptom complex simulates to a great degree the diarrhea noted by Gardner and his associates in rats deprived of potassium, with improvement following the administration of potassium salts.[18]

The explanation is not evident for utilization of the colonic route by the body to excrete chloride. A teleological explanation cannot be offered, but this case, the one reported by Gamble and his associates, and the one reported by Darrow stimulate interest in noting the true incidence of this bizarre phenomenon and its explanation.

SUMMARY

An entity of chloridorrhea is described. The patient expelled copious quantities of a watery diarrhea from a transverse colostomy performed for intestinal obstruction due to diverticulitis of the descending colon. The diarrhea was intrac-

table to ordinary methods of therapy and was aggravated by the intravenous administration of chloride. A remarkable feature of the stools was the presence of chloride in excess of sodium. Significant quantities of potassium were also present. Absorption of fat and nitrogen was apparently normal.

The watery diarrhea and chloridorrhea subsided after potassium salts were administered. There was an associated improvement in the patient's feeling of well-being and a return to normal levels of the plasma electrolytes (carbon-dioxide-combining power decreased and potassium level increased).

It is postulated that the chloridorrhea associated with voluminous watery stools may be an unusual expression of potassium deficiency.

The reason for the colonic route of excretion of chloride and the mechanism for transfer of chloride to the intestine remain enigmatic.

REFERENCES

1. Ariel, I. M.: The Internal Balance of Plasma Protein in Surgical Patients, Surg., Gynec. & Obst. **92**:405, 1951.

2. Ariel, I. M., and Kremen, A. J.: The Compartmental Distribution of Sodium Chloride in Surgical Patients Pre- and Post-Operatively, Ann. Surg. **132**:1009, 1950.

3. Ariel, I. M.: Abels, J.; Pack, G. T., and Rhoads, C. P.: The Treatment of Hypochloremia Refractory to the Administration of Sodium Chloride, Especially in Patients with Gastrointestinal Cancer, J. A. M. A. **123**:28, 1943.

4. Bennett, T. I., and Hardwick, C.: Chronic Jejunoileal Insufficiency, Lancet **2**:381, 1940.

5. Blumgart, H. L.: Three Fatal Adult Cases of Malabsorption of Fat, Arch. Int. Med. **32**:113, 1923.

6. Butler, A. M.; Talbot, M. B., and MacLachlan, E. A.: Effect of Testosterone Therapy on Concentration of Potassium in Serum, Proc. Soc, Exper. Biol. & Med. **51**:378, 1942.

7. Darrow, D. C.: Body-Fluid Physiology. The Relation of Tissue Composition to Problems of Water and Electrolyte Balance, New England J. Med. **233**:91, 1945.

8. Darrow, D. C.: The retention of Electrolyte During Recovery from Severe Dehydration Due to Diarrhea, J. Pediat. **28**:515, 1946.

9. Darrow, D. C.: Changes in Muscle Composition in Alkalosis, J. Clin. Invest. **25**:324, 1946.

10. Darrow, D. C.: Congenital Alkalosis with Diarrhea, J. Pediat. **26**:519, 1945.

11. Deane, N., and Smith, H. W.: The Distribution of Sodium and Potassium in Man, J. Clin. Invest. **31**:197, 1952.

12. Deane, N.; Ziff, M., and Smith, H. W.: The Distribution of Total Body Chloride in Man, J. Clin. Invest. **31**:200, 1952.

13. Dennis, C., and Visscher, M. B.: Studies on Rates of Absorption of Water and Salt from Ileum of Dog, Am. J. Physiol. **131**:402, 1940.

14. Earle, D. P.; Farber, S. J.; Alexander, J. D., and Pellegrino, E. D.: Renal Function and Electrolyte Metabolism in Acute Glomerulonephritis, J. Clin. Invest., **30**:421, 1951.

15. Elkinton, J. R.; Squires, R. D., and Crosley, A. P., Jr.: Intracellular Cation Exchanges in Metabolic Alkalosis, J. Clin. Invest. **30**:369, 1951.

16. Fairley, N. H., and Mackie, F. P.: The Clinical and Biochemical Syndrome in Lymphadenoma and Allied Diseases Involving the Mesenteric Lymph Glands, Brit. M. J. **1**:375, 1937.

17. Gamble, J. L.; Fahey, K. R.; Appleton, J., and MacLachlan, E. A.: Congenital Alkalosis with Diarrhea, J Pediat. **26**:509, 1945.

18. Gardner, L. I.; MacLachlan, E. A.; Terry, M. L.; McArthur, J. W., and Butler, A. M.: Chloride Diarrhea and Systemic Alkalosis in Potassium Deficiency, Fed. Proc. **8**:201, 1949.

19. Harrison, H. E.; Tompsett, R. E., and Barr, D. P.: Serum Potassium in Two Cases of Sprue, Proc. Soc. Exper. Biol. & Med. **54**:314, 1943.

20 Hastings, A. B., and Eichelberger, L.: The Exchange of Salt and Water between Muscle and Blood: I. The Effect of an Increase in Total Body Water Produced by the Intravenous Injection of Isotonic Salt Solutions, J. Biol. Chem. **117**:73, 1937.

21. Jones, I. D.: Is Lymphatic Obstruction a Factor in Sprue? Lancet **2**:525, 1924.

22. Lapides, J.: The Mechanism of Electrolyte Imbalance Following Ureterosigmoid Transplantation, Surg., Gynec. & Obst. **93**:691, 1951.

23. Mitchell, A. D., and Valk, W. L.: Hyperchloremic Acidosis of Ureterosigmoidostomies, J. Urol. **69**:82, 1953.

24. Mudge, G. H., and Vislocky, K.: Electrolyte Changes in Human Striated Muscle in Acidosis and Alkalosis, J. Clin. Invest. **28**:482, 1949.

25. Rosenheim, M. L., and Glynn, L. E.: Mesenteric Chyladenectasis with Steatorrhea and Features of Addison's Disease, J. Path. & Bact. **47**:285, 1938.

26. Sunderman, F. W., and Williams, P.: Analysis of Chloride in Tissues, J. Biol. Chem. **102**:279, 1933.

27. Wallace, W. M.: Improved Flame Photometer for Sodium and Potassium Analyses, Am. J. Dis. Child. **77**:104, 1949.

28. Wallace, W. M.; Holliday, M.; Cushman, M., and Elkinton, J. R.: The Application of the Internal Standard Flame Photometer to the Analysis of Biologic Material, J. Lab. & Clin. Med. **37**:621, 1951.

METASTATIC CARCINOMA OF RECTUM TO THE THYROID GLAND

Correlation with Radioactive Iodine Studies

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PHILADELPHIA

ALTHOUGH the gastrointestinal tract is the commonest site of carcinoma, the number of cases reported in which tumors from the gastrointestinal tract have spread to the thyroid gland is extremely small. Because we recently encountered a case of carcinoma of the rectum metastatic to the thyroid gland, we were led to examine the literature for other instances, and to date four such cases have been reported.

In 1939 Willis [1] collected 47 recorded cases of metastatic growths in the thyroid gland, of which 1 from the rectum was reported by Naegeli [2] in 1922. Willis added and described 10 personal cases, including another in which the primary tumor was in the rectum. In 1936 Rankin and Fortune [3] reported a case of carcinoma of the rectum in detail, which revealed, in addition to the customary metastases, one in the thyroid gland. At the Mayo Clinic [4] the collected cases until 1940 include only 1 case of primary carcinoma of the rectum which had metastasized to the thyroid gland out of a total of 19 cases of metastases involving the thyroid gland.

The case recently encountered is of interest because of its relative infrequent occurrence and because it was studied by means of radioactive iodine.

REPORT OF A CASE

In August, 1952, a woman, 73 years of age, was referred to this department with the chief complaint of hoarseness and shortness of breath of recent duration. The patient reported that she had a goiter for 50 years. Examination revealed a small pea-sized, round, smooth, firm mass in the region of the left upper lobe of the thyroid gland and a large almond-sized similar mass in the right lobe. No adenopathy was noted. Her past history revealed that an abdominoperoneal resection had been performed in October, 1945, for an adenocarcinoma of the rectum. A radioactive iodine uptake study showed a 5-hour uptake of 0%, a 24-hour uptake of 0%, and a 48-hour uptake of 8%.

The patient was laryngoscoped and found to have no intrinsic lesion of the larynx, but paralysis of the right vocal cord and pressure in the right supraglottic region were found. A diagnosis of a multinodular nontoxic adenoma of the thyroid was made; surgery was advised but refused by the patient. Her symptoms, however, gradually increased in severity and were accompanied by marked wheezing and, at times, stridor. She finally consented to surgery and was admitted to the hospital on Oct. 16, 1952. At this time the masses previously noted in the thyroid gland were larger, and a clinical diagnosis of carcinoma of the thyroid gland was made. The laboratory examination disclosed nothing of importance. Determination of the radioactive iodine uptake by the thyroid gland was repeated, and the urine excretion and the liver retention studies were performed according to the method recommended by Corrigan [5] (Charts 1, 2, and 3). In presence of carcinoma of the thyroid, it has been shown, there is a rapid decrease in

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activity at an abnormal rate after the initial rise in the iodine retention by the thyroid gland. The liver retention studies in patients with carcinoma of the thyroid gland show a gradually increasing liver count, and in urinary excretion there is a similar gradually rising excretion

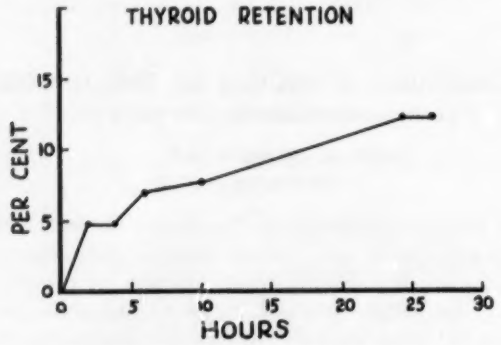

Chart 1.—Typically normal liver retention curve.

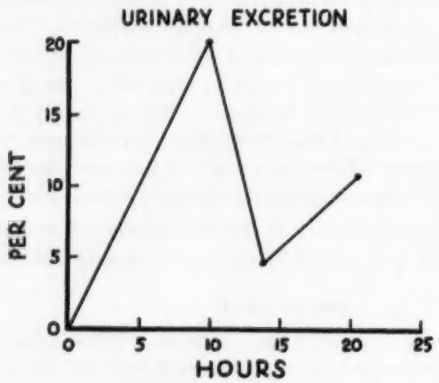

Chart 2.—Urinary excretion curve within normal limits.

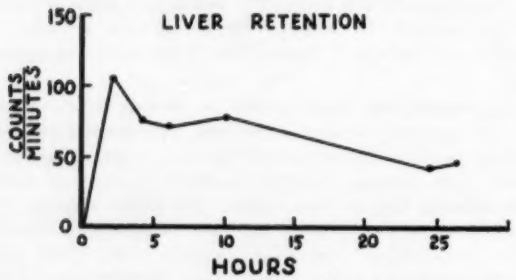

Chart 3.—Thyroid retention, typically normal.

curve. Since these findings were absent, we made the following report: "The results of this study do not conform with the usual results obtained in carcinoma of the thyroid gland. We therefore cannot confirm the clinical impression of primary carcinoma." X-ray studies failed

to reveal any evidence of metastasis or of substernal extension. The patient's dyspnea became increasingly severe, and an emergency tracheotomy was attempted. During this procedure, the patient died. An autopsy revealed the presence of metastatic adenocarcinoma of the rectum to the thyroid gland with extension to the larynx. The tumor almost completely replaced the right lobe of the thyroid gland and the isthmus. Recognizable thyroid tissue was present only within the anteroinferior portion of the tumor mass. The tumor infiltrated the length of the thyroid cartilage and impinged upon the larynx, reducing the lumen considerably. The thyroid tissue on the left side was scant. A small colloid adenoma is present on this side. No other evidence of metastasis was found.

COMMENT

The attention of pathologists has been attracted by the infrequency with which metastatic tumors are found in the thyroid gland. It has been suggested that this infrequency may be more apparent than real, since a careful study of the thyroid gland is seldom done on a routine autopsy. Willis [1] found metastatic lesions of the thyroid gland in 5.29% of cases in which death was due to carcinoma. Rice [6] found embolic tumor cells in 8 of 89 glands examined in cases in which carcinoma was the cause of death. It would appear that metastatic tumors are found with greater frequency in adenomatous glands than in normal glands. This was true in 12 of the 19 cases studied by Mayo and in our case also. No adequate explanation of this phenomenon has been forthcoming.

As the result of the metastatic lesions, marked metabolic changes have been described. Their range runs from myxedema, as found by Willis,[1] to toxic goiter, as reported by Mori.[7] Study of our case with I^{131} not only revealed a myxoedematous uptake by the thyroid gland but also the type of retention that did not confirm the clinical diagnosis of primary carcinoma of the thyroid gland.

This case, therefore, is unique in that the I^{131} studies were confirmed pathologically (absence of primary carcinoma of the thyroid gland) and that the patient died of asphyxiation, resulting from compression of the larynx by metastasis to the thyroid gland from an antecedent rectal carcinoma. It is of interest that seven years elapsed from the time of her abdominoperoneal resection to her recent metastasis and that this represented a single lesion with no local recurrence or other metastasis of the original carcinoma.

REFERENCES

1. Willis, R. A.: Metastatic Tumors in the Thyroid Gland, Am. J. Path. **7**:187-208, 1931.

2. Naegeli, T.: Matastasen eines Rectumcarcinoms in einem Schilddrüsenadenom, Zentralbl. allg. Path **23**:290-293, 1912.

3. Rankin, F. W., and Fortune, C. H.: Metastasis to the Thyroid Gland from Cancer of the Colon, Ann. Surg. **104**:36-40, 1936.

4. Mayo, C. W., and Schlicke, C. P.: Exogenous Tumors of the Thyroid Gland, Am. J. Path. **17**:283-288, 1941.

5. Corrigan, K. E., and Hayden, H. S.: Diagnostic Studies with Radioactive Isotope Tracers, Radiology **59**:1-18, 1952.

6. Rice, C. O.: Microscopic Metastasis in the Thyroid Gland, Am. J. Path. **10**:407-412, 1934.

7. Mori, T.: Über das Auftreten thyreotoxischer Symptome bei Geschwultstanomalien in der Schilddrüse, Ztschr. Path. **12**:2-24, 1913.

MASSIVE HEMORRHAGE FROM GASTRIC ULCER ERODING GALL BLADDER AND ANOMALOUS CYSTIC ARTERY

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IN THE last decade, surgeons have focused their attention increasingly on the problems concerned with management of cases with severe bleeding from gastric ulcer. Stewart,[1] Finsterer,[2] and others have adopted the attitude that any patient with massive bleeding from ulcer of the stomach and duodenum should be subjected to emergency operation, while Andresen,[3] Meulengracht,[4] and their adherents prefer nonoperative therapy in all such cases. As a matter of routine, we have chosen a middle ground, feeling that each patient with massive hemorrhage from ulcer should be followed closely by both internist and surgeon, with an initial trial of conservative treatment. Like Dunphy and Hoerr,[5] we attempt to select early in the course of the bleeding those patients who have the so-called fatal type of hemorrhage, and to advise emergency operation for these patients only. This selection is taxing to the best clinical judgment, and the criteria for such selection have been discussed elsewhere.[6] Perhaps the most important criterion[7] for emergency operation is recurrence of bleeding while the patient is hospitalized and being given a conservative regimen, or failure of bleeding to cease promptly with such a regimen.

The severe type of bleeding from gastric ulcer usually occurs from ulcers on the lesser curvature of the stomach because they tend to erode the left or right gastric arteries. Likewise, bleeding from duodenal ulcers is usually massive when the lesion is on the posterior wall and erodes the gastroduodenal artery or the superior pancreaticoduodenal artery. Adherence of a lesser curvature gastric ulcer to the gall bladder is not an uncommon operative finding, although rarely discussed in the literature. However, erosion of the cystic artery by peptic ulcer as a cause of massive hemorrhage has never been reported to our knowledge.

REPORT OF A CASE

A 45-year-old white man, on the afternoon of Dec. 24, 1952, while visiting his wife who was a psychiatric patient in the Roper Hospital, suddenly vomited a large amount of blood. He was immediately admitted to the hospital.

The patient had been in good health, but in 1944 dyspeptic symptoms had developed, and at that time it was said that an x-ray diagnosis of duodenal ulcer was made. After a limited period of medical therapy in 1944, his symptoms subsided entirely. In April, 1952, right upper quadrant pain had developed, which occurred particularly after meals, but this subsided one

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week after onset, without any treatment. For the week preceding admission, he had had pain in the right upper quadrant, particularly just beneath the right costal margin. This pain had been almost constant and not related to meals. On the day before admission, his physician had had a series of gall bladder x-rays done, and the gall bladder had failed to concentrate the dye. The past history was not remarkable except for the occurrence of the usual childhood diseases—an appendectomy in 1922 and a tonsillectomy in 1932. In 1949 he had been treated for a neuritis of both radial nerves, which had subsided with symptomatic treatment. His family history was of no significance, and a review of systems was essentially negative, except in relation to the present illness. He gave no history of previous melena, hematemesis, or jaundice. He smoked cigarettes fairly heavily and drank whiskey on social occasions only.

On admission the temperature was 99.6 F., pulse rate 92, and blood pressure 130/70. The mucous membranes and skin were pale. The nasal septum was deviated to the left. Several teeth were carious. There was moderate tenderness in the right upper quadrant just beneath the right costal margin, with rebound tenderness in that area, and peristalsis was not audible. No spasm was discernible. The remainder of the physical examination was within normal limits.

On admission the urinalysis was negative except for an occasional white blood cell and a trace of albumin. The packed-cell volume on admission was 32%. Shortly after admission, as a blood transfusion was being started, the blood pressure dropped, and his skin became moist and cool; he passed a large amount of dark blood by rectum, but the blood pressure and pulse rate returned to more nearly normal levels shortly after the blood transfusion was begun. He was given slowly 1,000 cc. of citrated whole blood intravenously, and during this time, although the blood pressure was sustained at a normal level, he became rather restless and combative and was controlled with considerable difficulty with the aid of barbiturate sedation. At this time he became temporarily irrational. After 2 pt. (1 liter) of blood had been received, six hours after admission the packed-cell volume was 35%. An additional pint of blood was given slowly, but the following morning, approximately 12 hours after admission, the packed-cell volume was only 28%. At this time the patient vomited up a large amount of coffee-ground material, his blood pressure dropped, and he again experienced a mild state of shock. During the preceding hours, in addition to the blood transfusions, he had been given a Sippy regimen (2 oz. [60 cc.] milk and cream every hour), 1 gm. of calcium gluconate intravenously, 5 mg. of sodium menadiol diphosphate (Synkayvite sodium diphosphate) intramuscularly, and Kolantyl Gel (an antacid and antispasmodic) 2 oz. every two hours. The prothrombin time on the day following admission was within normal limits.

Since 12 hours of a conservative regimen had failed to improve the patient's condition, the decision was reached to perform emergency laparotomy. A Levin tube was passed into his stomach and a moderate amount of old blood aspirated. Another blood transfusion was started and 1,000 cc. of blood was given rather rapidly. On arrival in the operating room at 1 p. m. on Dec. 25, 1952, he appeared to be in good general condition for the moment. With the use of general endotracheal anesthesia, cyclopropane and ether, the abdomen was entered through an upper right rectus paramedian incision. All of the small bowel and large bowel were found to be filled with blood. On the lesser curvature of the stomach, just proximal to the pylorus, there was a large (2.5 cm. in diameter) ulcer which had penetrated the wall of the ampulla of the gall bladder. When we attempted to dissect the stomach free from the gall bladder, the stomach wall was partially torn away from the ulcer base, and this separation was then completed so that the ulcer base remained on the gall-bladder ampulla. It then became apparent that in the center of this ulcer there was a small (3 mm. diameter) sclerotic vessel, the lumen of which was plugged by a fresh thrombus. When the thrombus was removed, the vessel spurted blood vigorously. This bleeding was promptly controlled by a suture ligature around the vessel. On further investigation and dissection in the gall-bladder area, it became apparent that this vessel was a large branch of the cystic artery, which arose in an anomalous position from the common hepatic artery at a point caudad to the position of the cystic duct. After triple ligation of the cystic artery and the cystic duct, the gall bladder was removed from above downward in the usual manner; a subtotal gastric resection was then carried out, removing approximately two-thirds of the stomach, and an antecolic (Hofmeister) gastrojejunal anastomosis was done, with the use of a loop of jejunum approximately 20 cm. distal to the ligament of Treitz. The abdomen was closed in layers

in the usual manner. During the procedure, which took approximately four hours, the patient received 1,500 cc. of blood intravenously, and he received another pint of blood on return to his room.

The pathology report (Dr. E. E. McKee) was as follows: The gall bladder has a thick indurated wall. Attached or fused to the serosal surface is a crater-like structure measuring an estimated 2.5 cm. in diameter, in the base of which is a small artery (Fig. 1). In a fresh state, the stomach contains a large quantity of currant jelly blood. In the lesser curvature is a thickened area which appears to represent recent incision and closure.

Sections show a chronically inflammed and thickened gall bladder wall. Fused to its serosal surface is a necrotic heavily inflamed crater of a gastric ulcer (Fig. 2). The base of this ulcer consists of granulation and scar tissue, and there is a prominent artery lying quite close to the surface and showing necrosis of the wall (Fig. 3). Other sections from the stomach show no significant changes.

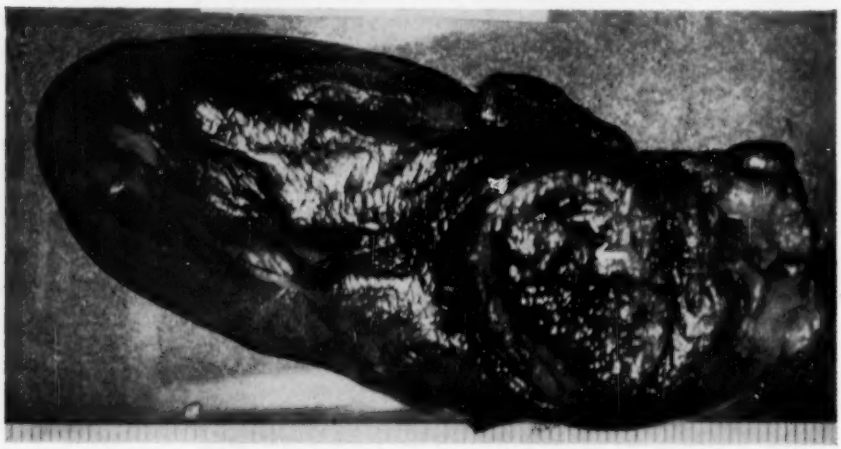

Fig. 1.—Gall bladder with gastric ulcer adherent to serosal surface. Arrow points to eroded artery which has been ligated.

The pathologic diagnoses were chronic ulcer of the stomach, with attachment of the gall bladder, rupture of the cystic artery, and chronic cholecystitis.

Postoperatively the patient did fairly well, the blood pressure and pulse rate remaining stable at normal levels. A mild basal atelectasis developed on the right, which responded to antibiotics, hyperventilation, and the usual conservative measures. The red blood cell count on the day following operation was 3,330,000, with 10 gm. of hemoglobin per 100 cc. During the next two days, he was given 500 cc. of blood each day, and on Dec. 28, the red blood cell count was 4,640,000, with 12 gm. of hemoglobin per 100 cc. After the third postoperative day, the temperature did not rise above a level of 99.8 F. The Levin tube was removed on the second postoperative day, and by the fifth postoperative day he was taking a five-meal soft diet satisfactorily. During the first two or three days of this diet, he had minor evidences of "the dumping syndrome," but after a few more days, the symptoms of sweating, nausea, weakness, and fullness after meals disappeared.

The patient was discharged on the 16th postoperative day. He did well at home until early in February, 1953, when he noticed the development of jaundice, dark urine, and alcoholic stools. He was again hospitalized on Feb. 16. On this admission it was noted that his liver was markedly enlarged and that there was a marked degree of jaundice. Results of liver function and other studies seemed to justify the opinion that this syndrome was based on homologous serum hepatitis.

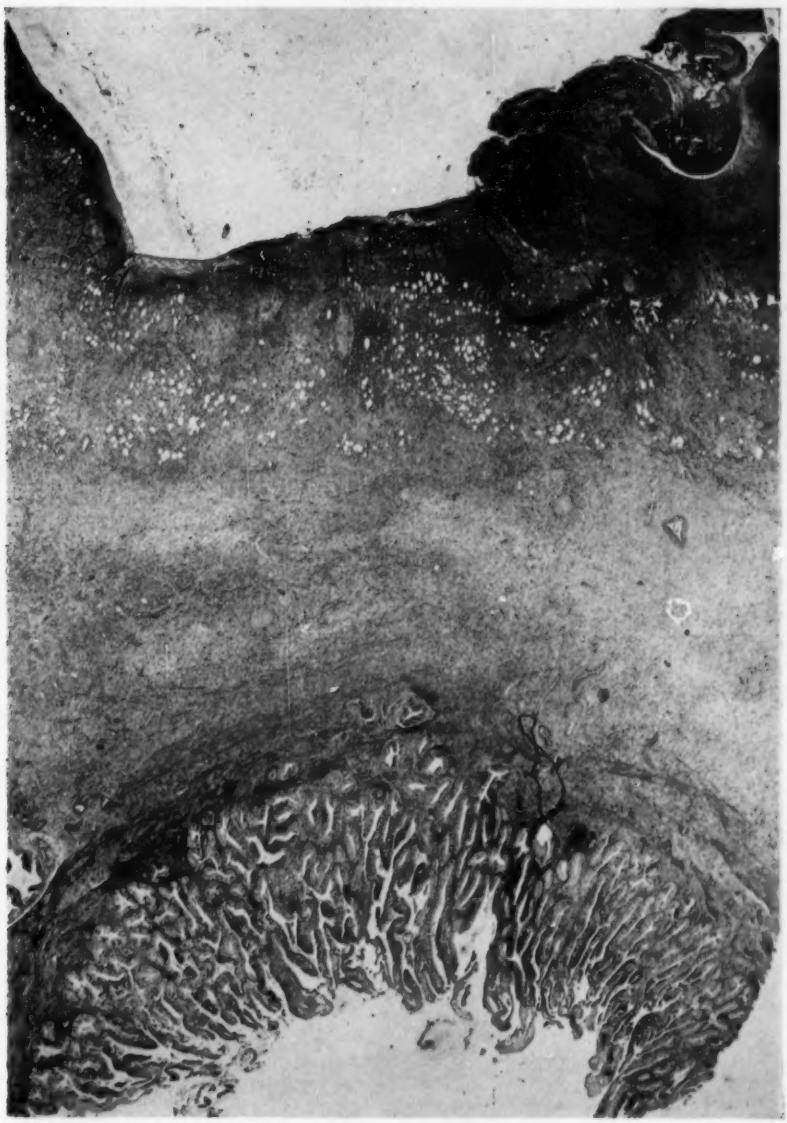

Fig. 2.—Photomicrograph (× 15) showing gall bladder mucosa at left and peptic ulcer at right.

Fig. 3.—Photomicrograph (× 50) showing large branch of cystic artery eroded by ulcer.

With use of a conservative medical regimen, the jaundice gradually subsided, and the patient's course in the hospital during a six-week period was one of slow, but progressive, improvement. At the time of discharge from the hospital on March 28, 1953, he was asymptomatic, eating well, and showed no definite evidence of jaundice. The stools and urine had regained their normal color, and the liver had subsided to normal size. He was again seen on May 16, 1953, at which time there was no evidence of icterus, and he was taking a regular diet in three daily meals, without any symptoms referable to the gastrointestinal tract. In July, 1953, he was working regularly and eating a normal diet.

COMMENT

Although as a rule we adhere to the principle of obtaining a roentgenologic diagnosis of peptic ulcer before emergency surgery is undertaken for severe bleeding, in the present case, the old history of duodenal ulcer seemed to be adequate. During the week preceding admission, the patient complained of right upper quadrant pain, which was quite different from the pain he had previously. It is interesting that the gall bladder failed to visualize on cholecystogram, and, although that organ contained no stones, there was considerable microscopic evidence of chronic cholecystitis. Erosion of the cystic artery by the ulcer penetrating the gall bladder would have been impossible except for the anomalous position of that artery, which ascended the inferior surface of the gall bladder. The viral hepatitis which developed approximately six weeks after operation was presumably transmitted by one of the many blood transfusions the patient received.

SUMMARY

A case of severe bleeding from a lesser curvature gastric ulcer penetrating the gall bladder and eroding the cystic artery is reported. Subtotal gastric resection and cholecystectomy as an emergency procedure was followed by recovery.

REFERENCES

1. Stewart, J. D.; Rudman, I.; Citret, C., and Hale, A. W., Jr.: The Definitive Treatment of Bleeding Peptic Ulcer, Ann. Surg. **132**:681-689, 1950.

2. Finsterer, H.: Surgical Treatment of Acute Profuse Gastric Hemorrhages, Surg., Gynec. and Obst. **69**:291-298, 1939.

3. Andresen, A. F. R.: Management of Gastric Hemorrhage, New York J. Med. **48**:603-606, 1948.

4. Meulengracht, E.: Fifteen Years' Experience with Free Feeding of Patients with Bleeding Peptic Ulcer: Fatal Cases, Arch. Int. Med. **80**:697-708, 1947.

5. Dunphy, J. E., and Hoerr, S. O.: The Indication for Emergency Operation in Severe Hemorrhage from Gastric or Duodenal Ulcer, Surgery **24**:231-238, 1948.

6. Sandusky, W. R., and Mayo, H. W., Jr.: The Management of Severe Bleeding from Gastric, Duodenal, and Jejunal Ulcers, South. Surgeon **15**:69-82, 1949.

7. Holman, C. W.: Severe Hemorrhage in Gastric and in Duodenal Ulcer: Study of 90 Cases, Arch. Surg. **40**:150-160, 1940.

LARGE BOWEL OBSTRUCTION CAUSED BY METASTATIC CARCINOMA ORIGINATING IN THE LARYNX

Report of a Case and Review of the Literature

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CARCINOMA of the larynx is considered a tumor "killing on the spot."[4] Metastasis from this neoplasm to other viscera is rare.* In order of their incidence, there are metastases to the lymph nodes, airborne implants along the respiratory tract and pharyngoesophagus, and blood-borne metastasis, which is the most unusual.†

This is a case report of a patient who died as the result of an obstruction of the transverse colon secondary to metastasis of a squamous cell carcinoma of the larynx.

REPORT OF A CASE

A 76-year-old man was admitted to Presbyterian Hospital, Denver, on Oct. 9, 1949. He complained of generalized abdominal pain, vomiting, and abdominal distention.

Eight months before he was admitted to the hospital on this occasion, his record showed, he had had a laryngectomy for carcinoma of the larynx, which had been symptomatic for two years. Convalescing uneventfully from this laryngectomy, he had adjusted to his permanent tracheotomy in a satisfactory manner. On Oct. 1, nine days before admission, the patient passed a tarry stool and felt weak for two days, but did not consider it essential to call his physician. The day before he was admitted to the hospital, he experienced an acute pain in the upper left part of the abdomen, vomited, and noticed that his abdomen became extremely distended.

Upon physical examination, the patient appeared acutely ill. He had a well-functioning permanent tracheotomy. There was no cervical adenopathy. His abdomen was distended and generally tender. Considerable tenderness and rebound pain could be elicited over the region of the cecum. His temperature was 100.4 F. The hemoglobin was 13.6 gm. per 100 cc.; erythrocytes numbered 4,320,000 per cubic millimeter, and the leucocyte count was 5,700. Urinalysis was normal. A chest roentgenogram showed no pathologic condition. A plain film of the abdomen (Fig. 1) showed the presence of free air and a distended proximal colon. In view of the degree of distention and the rebound pain over the cecum, an emergency decompression procedure was considered mandatory.

Operation was performed six hours after he was admitted to the hospital. Tetracaine hydrochloride, subarachnoid block, and cyclopropane were used for anesthesia.

The abdomen was entered through an incision which split the right rectus muscle. The cecum, ascending colon, and proximal half of the transverse colon were greatly distended. A purse-string type of suture was placed in the wall of the cecum, and the cecum was decompressed aseptically with a trocar. A 45 F. Pezzar catheter was sutured into the lumen of the cecum and inverted with three consecutive purse-string sutures. There was some free, bloody, peritoneal

* References 3, 4, and 6.

† References 3 and 4.

fluid; consequently, it was thought essential to explore the right side of the colon for a perforation. The antimesenteric border was discolored, but there were no demonstrable perforations. A fixed mass could be palpated just proximal to the splenic flexure of the colon. The cecostomy tube was brought through the great omentum and through a stab wound lateral to the main

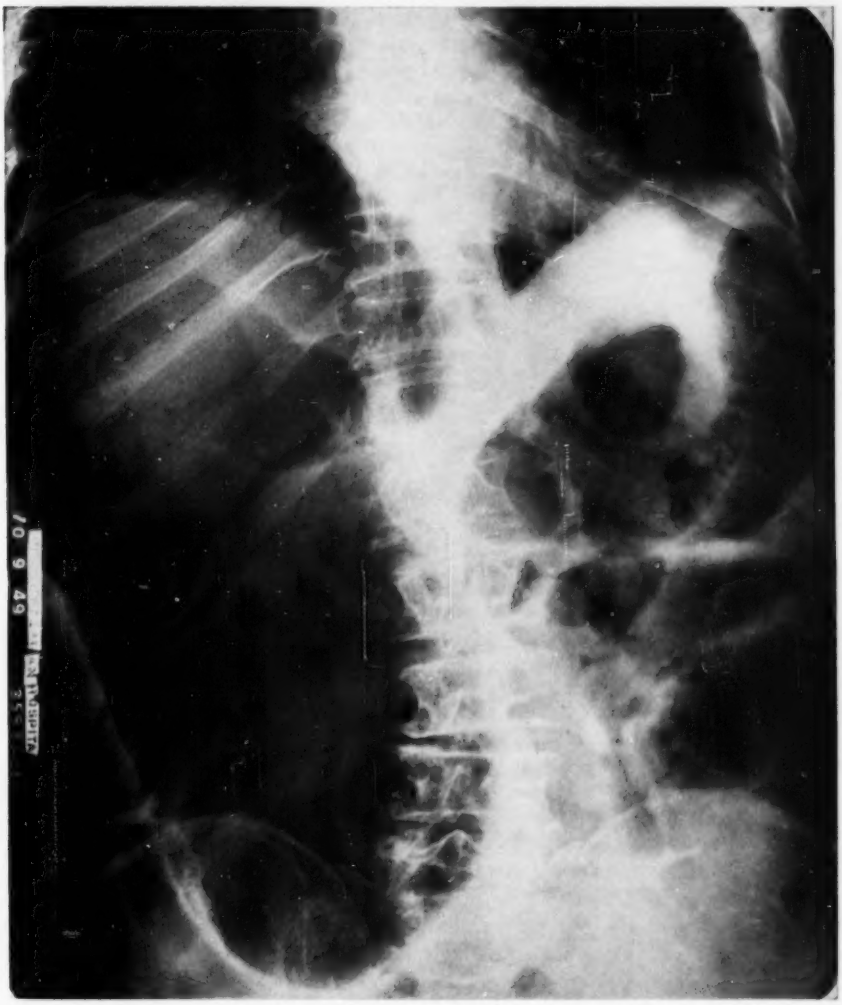

Fig. 1.—Roentgenogram taken on admission. The great distention of the right colon is the most prominent feature of this picture.

incision. The wound was closed in layers with absorbable surgical (gut) and nonabsorbable surgical (silk) suture material.

The patient's general condition was poor during the operation. He continuously received intravenous injection of fluids. His loss of blood was estimated and replaced.

The patient's postoperative course from the time of surgery to his death some 96 hours later was one of continuous battle against shock and respiratory difficulty. A chest roentgeno-

gram the day after operation revealed the presence of patchy bronchial pneumonia. A scout film of the abdomen at the same time showed very little air remaining in the proximal colon. A Miller-Abbott tube remained in the fundus of the stomach.

The patient's cecostomy functioned well. He was given 2,000,000 units of aqueous penicillin and 2 gm. of dihydrostreptomycin each 24-hour period.

His general condition deteriorated progressively. His temperature ranged from 100 to 103 F. except terminally, when it rose to 105 F. He excreted normal amounts of urine. He died at 9:25 a. m. on Oct. 14, 1949.

At autopsy the significant findings were bronchopneumonia and epidermoid metastatic carcinoma [2] of the lungs, liver, colon, small bowel, and lymph nodes. Grossly, the large annular lesion of the transverse colon appeared to be a typical "napkin ring" adenocarcinoma (Fig. 2); microscopically, however, it proved to be a metastatic epidermoid carcinoma (Fig. 3*b*) with the primary lesion in the larynx (Fig. 3*a*).

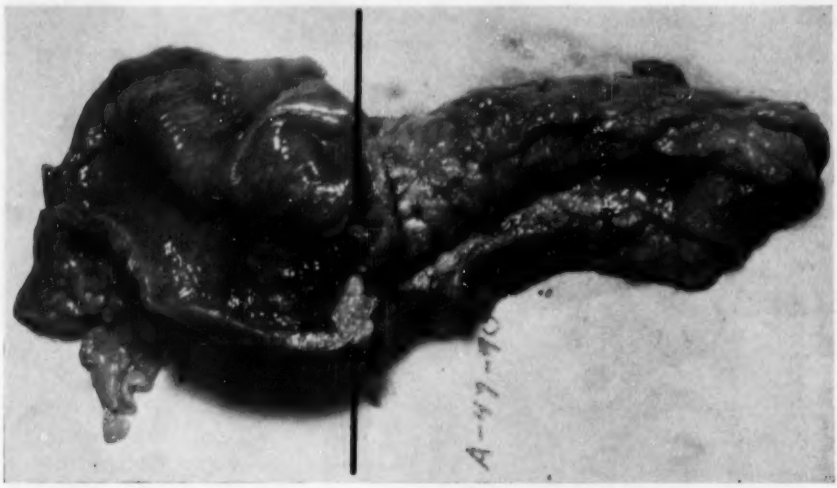

Fig. 2.—Macroscopic picture of the "napkin ring" lesion which had obstructed the transverse colon.

We have reported here one of the very few cases of a laryngeal cancer with blood-borne metastasis confirmed histologically. Terracol and Bringer,[4] in an excellent review of the international literature on the distant metastases of carcinoma of the larynx from 1878 through 1947, were able to find only 14 cases exhibiting multiple blood-borne metastases. Only eight of these cases wre histologically confirmed. The sites of metastases, as given in the same review, were lungs (10), liver (4), kidneys (3), esophagus (1), pericardium (1), cerebellum (1), hypophysis and sella turcica (1), soft palate (1), temporal bone (1), sternum (1), clavicle (1), scapula (1), spine (1), and femur (1).

Terracol and Bringer [4] also reviewed 21 cases with solitary metastasis to the digestive system. Only one of these cases with metastasis to the esophagus was proved histologically. It was probably implanted. A case of apparent metastasis to the colon was found to be adenocarcinoma, while the tumor of the larynx was squamous carcinoma. We have been able to find only one case of blood-borne metastasis reported in the literature after 1947.[3]

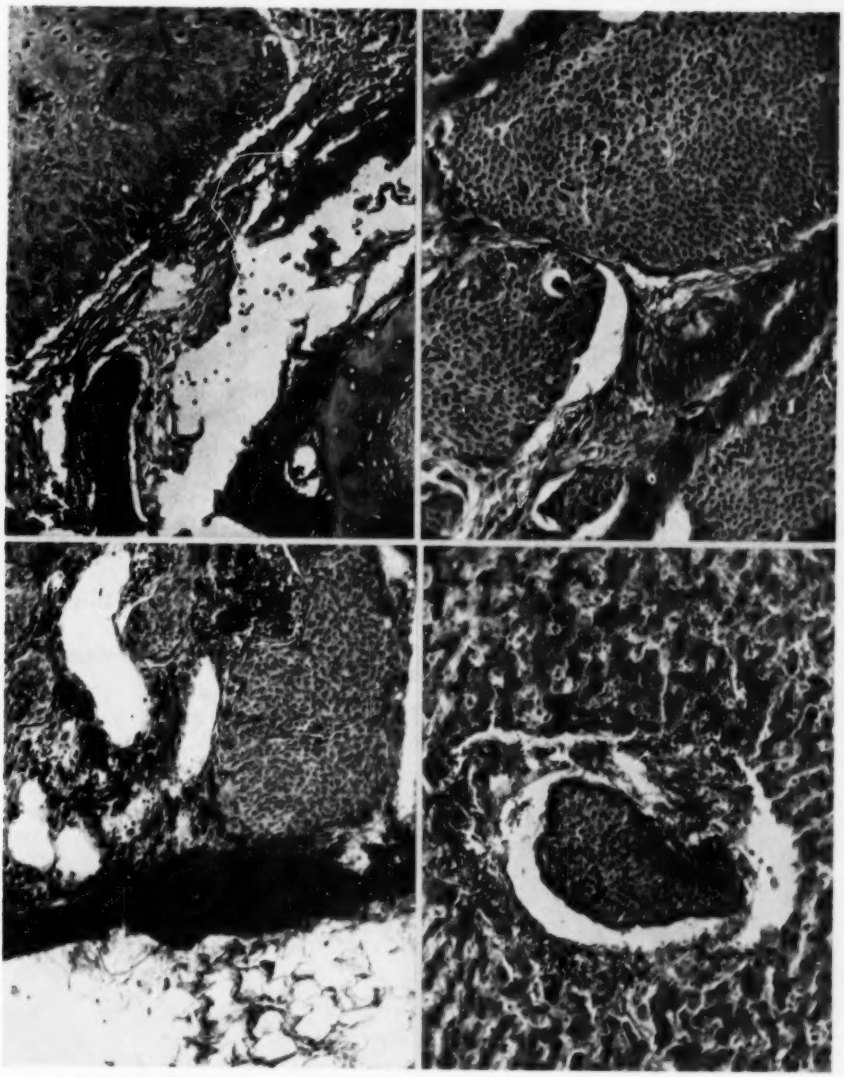

Fig. 3.—Microscopic pictures from the larynx (laryngectomy specimen), colon, lung, and liver (autopsy specimens); (*a*) epidermoid carcinomatous cells of the primary lesion occupy the left upper part of the picture, and laryngeal cartilage is seen at the right lower corner; (*b*) metastatic carcinomatous masses predominate in the muscularis of the colon at the site of the obstruction; (*c*) squamous metastatic element in a lung field; (*d*) embolic cancerous mass in the middle of liver parynchema.

In our cases, there were metastases to the colon and to the small intestine besides those to the lungs, the liver, and the regional lymph nodes.

The extrinsic type of cancer of the larynx is more frequently the source of metastasis than the intrinsic.‡ In our cases the tumor was intrinsic (subglottic).

The average time between the appearance of an epithelioma of the larynx and the appearance of metastasis is approximately one year.[4] In the case we reported the episode of obstruction of the colon occurred 33 months after the clinical appearance of the tumor and 8 months after the laryngectomy.

We think that in a case in which the clinical impression is that of a solitary blood-borne metastasis surgical treatment should be attempted because of the rarity of metastases in general.

1839 High St. (Dr. Sawyer).

‡ References 3 and 6.

REFERENCES

1. Fabbi, F.: Le metastasi del carcinoma laringeo, Oto-rin.-laring. ital. **20**:578, 1952.

2. Jackson, C.: Cancer of the Larynx, Philadelphia, W. B. Saunders Company, 1940.

3. Plauchu, M., and Potton, F.: Métastases ostéolytiques lointaines de cancer laryngé dans un tuberculeux pulmonaire, Lyon méd. **183**:369, 1950.

4. Terracol, J., and Bringer, C.: Les métastases lointaines dans le cancer du larynx, Ann. oto-laryng. **65**:1, 1948.

5. Thomson, St. C., and Colledge, L.: Cancer of the Larynx, New York, The Macmillan Company, 1930, Chap. 2.

6. Willis, R.: The Spread of Tumors in the Human Body, St. Louis, C. V. Mosby Company, 1952, Chaps. 2 and 6.

7. Work, W.: Carcinoma of the Larynx: II. Cervical Metastasis, Laryngoscope **62**:61, 1952.

Clinical Notes, New Instruments and Techniques

ADJUSTABLE FOOT RESTS

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The foot rest (*A*) consists of a board of five-ply wood connected to two flat steel bars and so constructed that a slot at the lower ends of the board permits it to slide or be moved on guide rails attached to the sides of a wooden box-like structure, as shown in Figure 1. The flat bars are connected to the board by wing nuts, which permit adjustment of the height

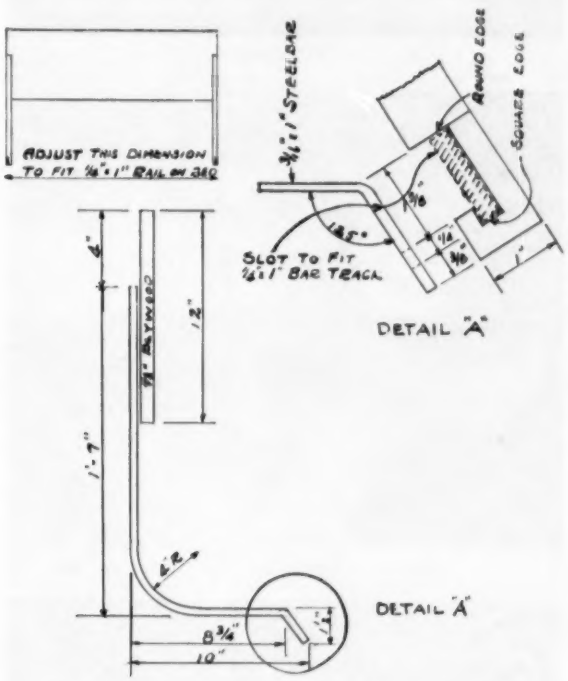

Fig. 1.—Schematic details of adjustable foot rests.

(Fig. 2). This structure is lined with a thin layer of sponge rubber. The device is so designed that the foot board can be brought up to the patient's paralyzed or affected feet simply by tilting the footboard and sliding it forward or backward as the case may require. To secure the foot rest in place it is pulled forward on the guide rails. This releases the engagement,

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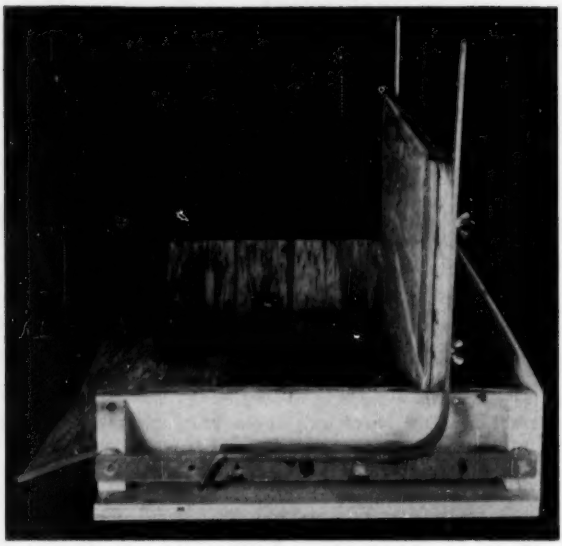

Fig. 2.—Model of adjustable foot rests.

Fig. 3.—Showing feet in position.

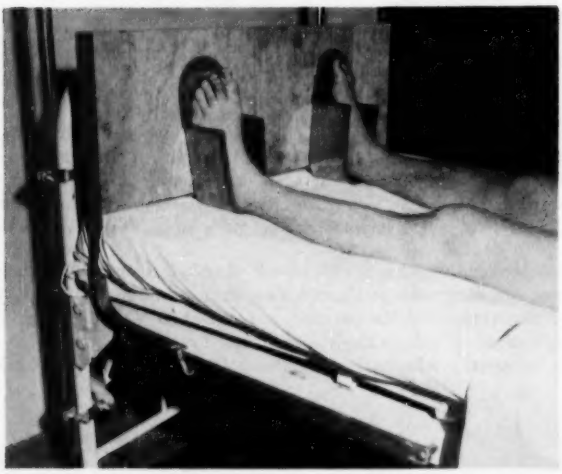

Fig. 4.—Foot rests mounted on hospital bed, with attachments.

and it is then dropped downward at the appropriate distance required. This procedure engages the slotted angle on the guide rail so that the foot board becomes fixed in one position (Fig. 3). Sufficient flexibility is present in the angular bars that plantar flexion movements of the feet can be carried out.

Another foot rest, shown in Figure 4, is a variation of the first (*A*) and consists of a laminated plywood board bolted to two steel angular bars. These angular bars have been described previously, the important feature being the slotted inferior end of the bar. As can be seen

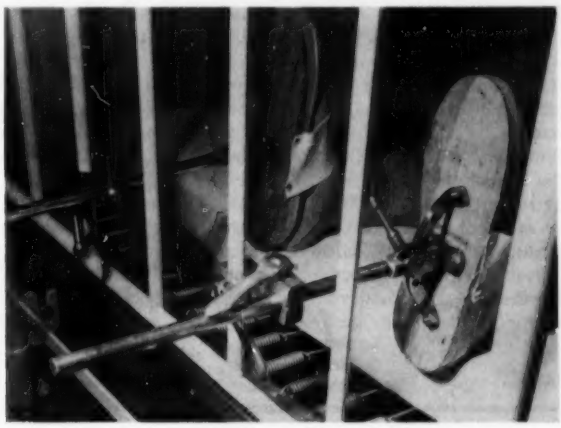

Fig. 5.—Foot rests for spastic limbs.

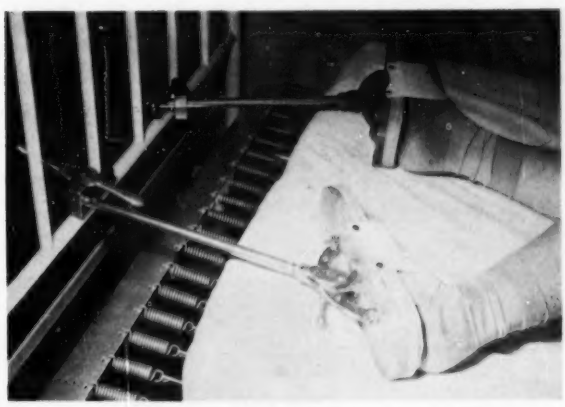

Fig. 6.—Position of foot rests when patient assumes lateral position.

from the photograph, it is important to have the angle and slot so constructed that it will ride on the guide rails when tilted. When the foot rest is in the vertical position, the sharp edge of the steel bar adjacent to the angle bites into the bottom of the guide rail, thus maintaining its position at that point. The guide rails are attached to the sides of the steel frame of a bed with bushings of the proper length. An additional feature is the boot-shaped foot attachments which support the feet and ankles in proper alignment. These foot attachments are connected to the laminated plywood by bolts soldered at its base.

The foot rests shown in Figure 5 are somewhat different from the previous ones, as they maintain the feet in position more rigidly through the medium of several mechanical features.

The essential units of this device consist of wooden shower clogs lined with sponge rubber with an elastic webbing to hold the feet in place. A solid steel bar, connected to the clog by means of a metal arc, serves as an axis and has a locking device. This arc permits dorsiflexion and plantar flexion. The other end of this bar is held near the foot of the bed with a clamp-like universal joint. In addition, this universal joint is also attached to the bed and thus maintains the steel bar in position and makes it possible for rotation and lateral movement to occur in the lower limbs.

PURPOSE AND USE

These foot rests are designed to maintain dorsiflexion of the feet either in patients with paralysis or in those confined to bed for long periods. It prevents "dropped feet." Early plantar flexion exercises can be instituted if active motion is possible.

The foot rest (*A*) is portable and can be used on any bed simply by placing it on top of the sheet and mattress. Plantar flexion resistance exercises can be carried out when prescribed, as the flat bars are flexible enough to bend with moderate motion of the feet.

The variation of the foot rest, described previously, is designed to maintain the feet in proper position when the body is turned to either side (Fig. 6). The boot-shaped foot pieces are lined with sponge rubber. They permit rotation should the patient assume the lateral position. Hand towels may be placed in these foot pieces for sanitary purposes. This foot rest is suitable for patients with poliomyelitis, paraplegia, and orthopedic conditions requiring immobilization.

The rigid foot rest (Fig. 5), is designed to maintain the feet in proper position when spasticity or contractures of the lower extremities are present. The device offers many possibilities for varying the position of the feet, e. g., the side-lying position, and yet prevents deformities from occurring.

CORRECTION

In the article by Drs. George O. Baumrucker and Jesse W. Shaw, "Urological Complications Following Abdominoperineal Resection of the Rectum," in the October, 1953, issue of the ARCHIVES, the dose of bethanecol (Urecholine) chloride was incorrectly stated (page 511, line 5). The dose should have been 5 mg. instead of 5 gm.

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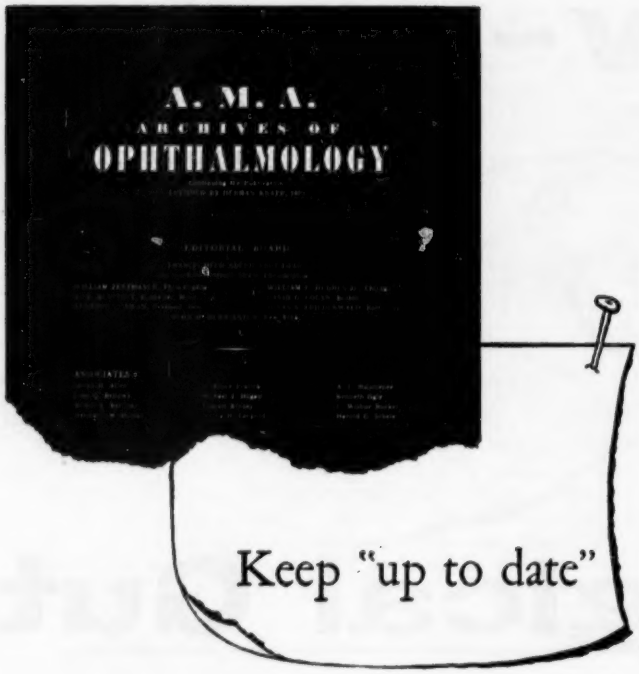

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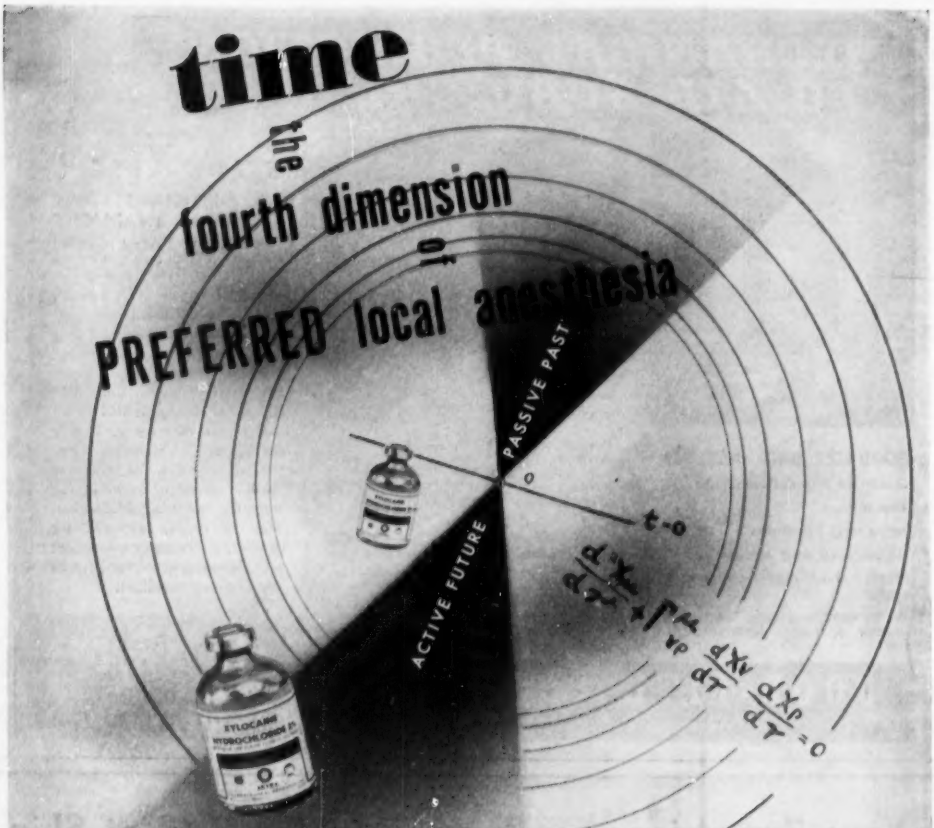

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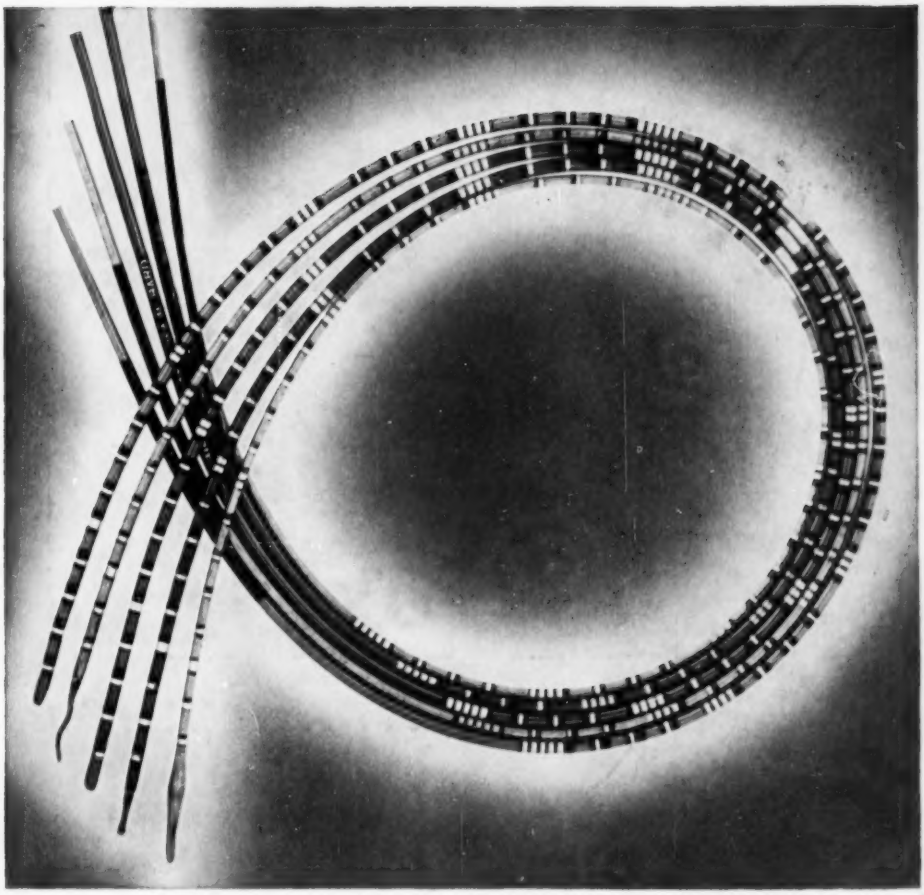

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